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Acupoint embedding therapy

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Abstract

Background: Peripheral nerve trauma remains a major cause of motor disability, at the same time functional restoration after treatment continues to show modest results. Acupoint embedding therapy is a type of acupuncture treatment in which different biodegradable materials are inserted into specific points for long-term stimulation. It has a good analgesic effect in chronic pain, and it is considered a cure for many diseases. Different biodegradable materials have been developed and widely used. Catgut has a good biodegradability and low price, but it could cause infections and having unstable chemical properties had been limited in clinical use. Such synthetic materials as polylactic acid and polyglycolic acid present low-cost, good biodegradability and biocompatibility compared with the catgut. However, their poor hydrophilicity and cell adhesion limited their therapeutic efficacy. The ideal embedding materials are required to be safe, non-toxic, biocompatible, and to have excellent swelling and biodegradation behaviors. Acupoint embedding therapy can be a promising treatment method of peripheral nerve disorders.

Conclusions: Acupoint embedding therapy is an invasive treatment which can prolong point stimulation, reduces the frequencies of pain and psychological fear of patients. It seems to be a promising method of neuropathy treatment. The properties of the filaments for acupoint embedding therapy can be improved by surface modification technologies.

Key words: acupuncture embedding therapy, neuropathy.

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Introduction

Acupuncture is generally held to have originated in China, being first mentioned in documents dating from a few hundred years leading up to the Common Era. Sharpened stones and bones that date from about 6000 BC have been interpreted as instruments for acupuncture treatment [1, 2].

The first medical description of acupuncture by a European physician was by Ten Rhijne, in about 1680, who worked for the East India Company and witnessed acupuncture practice in Japan [3, 4].

In 1960s, there appeared a treatment method by implanting absorbable materials (e.g. catgut) substituting for filiform needles into the acupoints, which realized long-time needle retaining and also avoided the danger of filiform needle retaining. This method was then termed acupoint thread-embedding therapy. During recent years, by constant improvement of embedding apparatus and materials, this method has gradually evolved to be micro-invasive thread-embedding therapy [5].

Traditional acupuncture. Acupuncture is a medical intervention in which fine needles are applied to specific parts of the body, called acupuncture points (or acupoints) and penetrated through the muscular or other subcutaneous layers. According to the theory of traditional Chinese medicine, acupuncture modulates the flow of Qi and blood through the meridians and restores the balance of the five organs to maintain homeostasis [6]. Each acupoint has its own specific therapeutic actions. They are presumed to be pathophysiologically associated with and possibly reflect the status of visceral organs and systemic conditions, and thus the stimulation of specific acupoints may evoke the responsiveness that controls the unbalanced internal milieu and improves body symptoms. Acupuncture stimulation is given right on the acupoint or a nearby affected area "*ashi point*" for the treatment of local symptoms, whereas distal acupuncture stimulation is applied to treat diseases in the internal organs and systemic abnormalities [7].

In manual acupuncture, an acupuncturist penetrates the skin with a metallic needle and manipulates it by rotating in one or both directions or lifting and thrusting [8]. Between 5 and 15 needles are used in a typical treatment, with the point combinations varying during a course of sessions [9]. It is known that during acupuncture practice, acupuncturists experience a special touch sensation perceived as heaviness, tenseness, or terseness, and patients perceive feelings of numbness, heaviness, soreness, and distention around the site of needle stimulation. These are called *deq*i sensations. Clinical data further indicate that patients frequently feel *deqi* sensations spreading to other parts of the body [10, 11].

In electric acupuncture, a small electric current is applied to pairs of acupuncture needles [8]. To maximize therapeutic effects, acupuncture is usually practiced first by applying manual acupuncture to evoke *deqi* sensation and followed by electrical stimulation for 15–20 minutes [10]. Traditional acupuncture therapy has the advantages of safety, validity and non-toxic side effects, but with and unexpected short function time and frequent operation [12].

Among acupunctures, there mainly are filiform needles, electric needles, hydro-needles (small dose point injection), fire needles, warm needles, skin needles (including plum-blossom needles), ear needles, prick blood-letting therapy and many others [13].

According to the World Health Organization, acupuncture has been shown to be an effective alternative or complementary treatment to 28 diseases, symptoms, or conditions [14].

Peripheral neuropathy is broadly defined as damage of the peripheral nervous system caused by a primary lesion or dysfunction [15]. The recovery of peripheral nerve injury is a long and slow process. This may be because of the period of time needed for neural regeneration and functional reconstruction, but treatment methods may also contribute to the delay in recovery [16, 17]. Peripheral neuropathy, particularly when it involves the large nerve fibers, is ideally suited for a localized structural needling approach. Needles placed in close proximity to a nerve stimulate the nerve fibers directly, with an electric current or a physical stimulus from manual acupuncture [18].

He et al. note that nerve injuries affect the metabolic microenvironment. Citing an example, they note that sciatic nerve injuries reduce acetylcholinesterase activity in the lumbar spinal cord microenvironment. This causes neuronal cell death thereby impeding nerve repair. The researchers note that acupuncture counteracts this effect citing that it successfully increases "acetylcholinesterase expression in spinal cord tissue after peripheral nerve injury". As a result, this may be an important mechanism by which acupuncture promotes the healing of peripheral nerves [19].

Lu et al. revealed that acupuncture and electroacupuncture could accelerate the maturity of regenerated nerves with larger mean values of axon number, endoneurial area, blood vessel number, and blood vessel area as compared with the controls [20].

Acupuncture is an established adjuvant analgesic modality for the treatment of chronic pain, and it is considered a cure for many ailments and disorders [21]. It is thought to stimulate inhibitory nerve fibers for a short period, reducing transmission of pain signal to the brain [22]. Acupuncture treatment activates endogenous analgesic mechanisms [23], causing secretion of endorphin which is an endogenous opioid [24] and triggering release of adenosine [25], producing a rapidly effective analgesic action. Extensive research has shown that acupuncture analgesia may be initiated by stimulation of high-threshold, small-diameter nerves in the muscles [26].

Han et al. found that acupuncture can promote release of neurotransmitter such as 5- hydroxy tryptamine and in addition it generates neuropeptide through electrical stimulation of different frequencies that has significant effect to pain reduction [27]. Park et al. speculate that acupuncture stimulation may trigger the responsiveness of sensory receptors and generate neural activity in its own specific way, which may be encoded in the cerebral cortex and autonomic neuronal center and exert its effects on regulating inflammation. Future investigations to explore whether acupuncture-specific vagal activity exists and acts on cells in target organs will be of great importance to gain insights into the mechanistic basis of acupuncture [7].

Acupuncture may elicit vegetative reflexes, thereby changing the flow of blood and enhancing functional properties of connective tissue and organs [28]. Litscher et al. showed that acupuncture may increase blood flow in the limbs [29]. Increased blood flow to the vasa nervorum and dependant capillary beds supplying the neurons [30] may therefore contribute to the immediate effect of acupuncture [28]. Over some time, these may contribute to nerve repair with measurable improvement of axons or myelin sheaths after 10 treatments. Local and central effects on vascularization may thus represent combined causes for regeneration [31, 32]. Acupuncture could regulate multiple molecules and signaling pathways that lead to excitotoxicity, oxidative stress, inflammation, and neurons death and survival and also promote neurogenesis, angiogenesis, and neuroplasticity after ischemic damage [33].

Risk factors for complications of acupuncture:

– For pregnant women, avoid needling points on the abdomen and lumbar region, and certain points known to cause strong sensations;

– Hemophilia can affect clotting factors;

– Advanced liver disease could compromise production of clotting factors;

– Patients taking blood thinners could bleed for longer periods;

– Patients with HIV infection or immunocompromised patients are at increased risk of opportunistic infections;

– Patients with diabetes are subject to poor wound healing; neuropathy can reduce sensory ability, leaving them at increased risk of undetected infection;

– Patients who have had transplants often take immune suppressants that make them prone to infections;

– High-dose steroids suppress the immune system;

– Open wounds increase risk of infection;

– Hypoglycemic, nervous, or very fatigued patients might faint.

Potential adverse events associated with acupuncture are: fainting during treatment, nausea and vomiting, increased pain, diarrhea, local skin irritation, headaches, sweating, dizziness, aggravation of symptoms, needle breakage.

Rare complications include: pneumothorax, spinal cord injury, septicemia, punctured organs, convulsions, argyria [34].

The most adverse effects associated with acupuncture are minor and serious complications are rare. Patients should be forewarned of potential common, though minor, adverse effects. Needle penetration might cause pain and bleeding. Reports of fainting remind practitioners that patients might be better off prone than sitting during treatments. Practitioners should keep some potentially fatal effects in mind when patients report shortness of breath, pleuritic chest pain, or fever after acupuncture treatment. All acupuncture practitioners should have proper training in techniques and safety [34].

Acupoint embedding therapy

In traditional Chinese medicine, catgut-embedding therapy has been used for the treatment of several diseases such as musculoskeletal pain, obesity, chronic urticaria, perimenopausal syndrome, depressive neurosis and others [35]. It is special type of acupuncture that inserts medical threads into skin, subcutaneous tissue or muscles at specific points [36]. Although acupoint catgut embedding therapy is considered an invasive treatment from a western medicine perspective, it has attracted considerable attention from clinicians in China due to its easy operation and durable stimulation, and has been widely used in recent years. Suture buried in acupoints can produce persistent stimulation on the basis of selecting sutures and acupoints according to deficiency and excess, which aims to regulate *yin* and *yang*, dredge the channels and collaterals, and reinforce the antipathogenic *Qi* and eliminate the pathogenic *Qi*. It has dual rapid and continuous action for chronic diseases. It is the combination of a variety of therapies (acupoint blocking, acupuncture, pricking, the after effect of tissue injury, needle retention). The intensity of stimulus would be changed with the time and the special needles and sutures can produce stronger efficacy than conventional acupuncture on controlling mind (*shen*) to facilitate *Qi* flow and dredging the meridian to regulate *Qi* and blood [37].

The effects of acupoint catgut embedding therapy in Western Medicine are similar to those of manual acupuncture. It provides both physical and chemical stimulation [38, 39].

The absorbable surgical thread, a foreign protein, can induce allergic reactions and the combined effects of proteolytic enzymes and macrophage action against the absorbable surgical thread may strengthen and extend the acupoint stimulation for 15–20 days as a consequence of the mild irritation in subcutaneous tissue, inducing a more persistent and potent physiological stimulation produced by the suture at the acupoints [39]. Acupoint embedding therapy improves body's nutrient metabolism and promotes blood circulation [37].

By using the specially made disposable embedding needle, the operation of micro-invasive thread embedding can be completed swiftly and conveniently in the way of injection. The embedding needle has a handle to hold and allows rapid inserting by only a hand. The mechanical spring ensures successful embedding of the thread. The marks on the needle body make it easy to control the inserting depth. The whole operation only takes 5-10 min, as only the thread not the needle needs to be retained. The stimulation produced by the retained thread can last for 1-2 weeks, during which the patients can move freely without any influence on their life. Therefore, this method can be applied in clinic safely for patients' convenience and less pain [40].

Patient should be informed about the local pain during operation and the postoperative reaction.

After the insertion, may occur such reactions as: a) the local skin will manifest redness, swelling, hotness and pain of aseptic reaction; b) hematoma may occur due to the needling injury and thread; c) general response with a fever of about 38^0C in 4-24hs, or even persistent high fever [37].

Thread-embedding acupuncture is a new subtype of acupuncture treatment developed from catgut-embedding therapy [35]. Different biodegradable materials have been developed and widely used. They are divided into natural and synthetic types according to material sources. Both of them have advantages and disadvantages [41]. For instance, natural embedding material is inexpensive and plentiful, but it also easily leads to an infection reaction due to poor biocompatibility. Hence, it has a higher applied risk due to the instable quality [42]. In contrast, synthetic embedding materials, such as polyglycolic acid [43] and polylactic acid [44], offer an excellent biodegradability and biocompatibility, and have a stable property through the whole implanting period. But their poor hydrophilicity and cell adhesion, inevitable large dimensions for producing a lasting effect largely affected their therapeutic efficacy in clinical application [45, 46].

There is a number of uncertainties, including the spinning speed, drawing temperature and stretching ratio, which affect compression behaviors in the preparation process of acupoint embedding monofilaments [47]. In addition, rigid acupoint embedding monofilaments will stimulate the subcutaneous tissue of the human body, resulting in a greater sense of pain for patients in clinical application. In contrast, soft acupoint embedding monofilaments may lead to difficulties in the embedding operation [48]. However, there is still a lack of relative study and a unified standard for a test method for monofilament compression behaviors [49].

The ideal embedding materials are required to provide properties such as safety, non-toxicity, good biocompatibility and absorbability [50, 51]. Antibacterial properties are essential in the prevention of infections [52, 53]. Also, embedding materials should provide enough mechanical properties to be implanted into the body and support peripheral nerve tissue [54]. Through good swelling behavior they are able to produce enough stimulus degree *in vivo*, yet retain a relatively small dimension *in vitro* and avoid the significant trauma [55]. Favorable hydrophilicity is also important for embedding material to adhere cells and work well in the human body [56].

Discussion

Catgut is a protein fiber of biological origin, that is derived from the small intestines of animals, mostly sheep or oxen [56]. Not many studies have investigated the mechanism of catgut implantation at acupoints. Li et al. explored the probable mechanism focusing on neurogenic inflammation [57]. Some studies have demonstrated that nerve stimulation could induce leukocyte activation and plasma extravasation, which is termed neurogenic inflammation [58, 59]. The mechanisms involve the regulation of nerve conduction, signal pathways, hormone level, protein expression, oxidative stress level, and structure restoration. The treatment generally regulates some specific biochemical factors to influence particular signal pathways, eventually controlling the apoptosis and proliferation of cells and repairing the damaged structure [60]. The mechanism of acupoint catgut embedding regards catgut as a type of heterogeneous protein, after inserting it into acupoints, its process of softening, decomposition, liquidation and absorption can effectively promote and enhance the nutrition metabolism, stress ability of bodies, vascular permeability and blood circulation [61]. Areas of catgut suture degradation contain dense accumulation of macrophages, lymphocytes, and foreign body giant cells. After complete absorption, these are replaced by a dense mass of macrophages [62]. Most studies indicate that catgut sutures are completely absorbed between 35 and 60 days [63]. However, the safety of catgut embedding has not yet been established, since it can cause various immune reactions, including allergic reactions and a subcutaneous nodule [64].

Polydioxanone (PDO) has been used in acupoint embedding therapy devices in Korea. It is a synthetic monofilamentous polymer made of polyester or a polymer of polydioxanone. PDO retains 50% tensile strength after 4 weeks, takes 180 days to be absorbed, and also has low tissue reactivity [65]. In Korea, the embedding of PDO thread at certain acupoints is widely used in the clinical practice for the treatment of chronic musculoskeletal pain. Nevertheless, the current level of evidence supporting the efficacy of embedding with PDO thread for patients with chronic musculoskeletal pain is insufficient [66]. Only case studies on the application of PDO embedding therapy for the patients with chronic low back pain treatment [67], shoulder pain [68], and osteoarthritis of the knee [69] have been published. In addition, no randomized clinical trials using PDO thread embedded as a sham-controlled intervention have been reported [70].

Polyglycolic acid (PGA) has held great promise for various biomedical applications in human tissue due to its advantages of being easily available, low cost and having excellent biodegradability and biocompatibility [71]. PGA monofilaments prepared by melt-spinning technology for acupoint embedding therapy materials have exhibited sufficient supply, good formation capacity and versatility in terms of surface functionalization [72, 73]. The PGA monofilament is considered to be a highly promising biodegradable material for ideal acupoint embedding therapy material preparation [74, 75]. PGA is broken down by hydrolysis into its respective acids and alcohols. It tends to lose mechanical strength rapidly, over a period of 2–4 weeks after implantation [76]. Some shortcomings were discovered and they may increase the risk of PGA implantations, such as insufficient hydrophilicity and cell adhesion caused by the relatively smooth surfaces [45]. These features are believed to be the main contributors to the unfavorable characteristics [77].

Polylactic acid (PLA) is one of the highest consuming bioplastics in the world. It is an aliphatic polyester obtained from renewable sources such as corn sugar, starch, potato, and sugarcane. PLA has 37% crystallinity, elongation at break 30.7%, glass transition temperature of 53°C, and a melting temperature ranging between 170–180°C [78]. It is used in the biomedical area, and has also begun to be applied as an embedding material for curing osteoporosis [79] and pseudo-myopia [80] and other diseases. However, its long degradation time (about 2 years) and poor hydrophilicity have limited its further application in acupoint embedding therapy [81].

Polylactic glycolic acid (PLGA) is polymerized by 9 polyglycolic acids (PGA) and one polylactide acid (PLA). It is simple in composition without bioproteins, and is now widely used as embedding material for its proper rigidity. When implanted in the acupoint of human body, it can produce a long-time stimulation which is similar to that produced by a filiform needle [82]. Histologic examination showed that the PGLA sutures were absorbed within 90 days [83], which might be the underlying mechanism of persistent analgesic effects [84]. PGLA has good biocompatibility, and no adverse reactions have been reported. Hydrophilicity, cell adhesion and degradation properties can be improved by surface modification technologies [85].

Surface modification technologies

Currently, there are numerous surface modification technologies, such as dip-coating, ultrasound, chemical vapor deposition, ion beam injection and surface graft polymerization, that can be applied to biomedical materials [86, 87]. Wang et al. attempted to use ultrasound treatment to modify PGA and polylactic-glycolic acid (PLGA) fibers, and the results suggested that both PGA and PLGA fibers achieved better hydrophilicity and cytocompatibility, while the tensile strength of PLGA increased and that of PGA changed little [88]. Among a variety of surface modification technologies, cold plasma modification has been regarded as one of the simplest and highly effective methods to modify biomaterials. It can promote the formation of new oxidized functional groups by introducing potential activation sites on their surfaces, and modify the remaining original properties of materials to a great extent without damaging their outermost surfaces [89, 90]. Song et al. point out that the photo-degradation, thermal, and microbial biodegradable properties of the PLA films can be significantly improved by plasma modification [91].

It is reported that solution dip-coating is one of the most widely used processes in textile manufacturing and the simplest functionalization technique for material surfaces, and chitosan is a promising natural compound, which possesses a prospective future due to its advantages of non-toxicity, antibacterial properties, biocompatibility, biodegradation and swelling properties [92, 93]. Chitosan is a linear, high molecular weight heteropolysaccharide [94], consisting of N-acetyl- glucosamine and N-glucosamine units [95]. With its abundant reserve, chitosan is the second most important natural polymer globally (the first is cellulose) and has been widely extracted from marine arthropods (prawns, crabs, shellfish, etc.) [96]. Hence, numerous chitosan coating applications on tissue engineering areas have been reported. Dubnika et al. used chitosan as an antibacterial agent to functionalize scaffolds and achieved a significant effect [97]. Niekraszewicz et al. used chitosan to modify polypropylene (PP) mesh and achieved good results in terms of mechanical and chemical properties; the biological purity was also improved [98]. Umair and colleagues reported that the PGA suture using N-halamine-based chitosan agents, its antibacterial efficacy was enhanced and could kill both *E. coli* and *S. aureus* bacteria within 15 min of contact time [99]. However, there is still a lack of detailed research about chitosan coating methods of monofilaments and existing studies prefer to target the biocompatibility, proliferation capacity, etc. Meanwhile, there are few reports on the self-swelling behaviors of embedding materials improved by chitosan coating [100].

Conclusions

1. Acupoint embedding therapy is an invasive treatment which can prolong point stimulation, reduces the frequencies of pain and psychological fear of patients and visits to the doctors.

2. The acupoint embedding therapy seems to be a promising method of neuropathy treatment.

3. The ideal embedding materials are required to provide properties such as safety, non-toxicity, good biocompatibility, excellent swelling and biodegradation behaviors.

4. The properties of the filaments for accupoint embedding therapy can be improved by surface modification technologies.

5. It will be great if the embedded material has also an antibacterial or active factor releasing effect which can be achieved by dip coating with chitosan or other substances.

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OI designed the trial, wrote the fist draft of manuscript. OP interpreted the data. VN revised the manuscript critically. All the authors revised and approved the final version of the manuscript.

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No approval was required for this review study.

Conflict of Interests

No competing interests were disclosed.