Clinical Practice of EECP in Non-Cardiac Disease in China
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Introduction
Enhanced external counterpulsation is a technique using a set of cuffs that are wrapped around the lower part of the body. During treatment, pressure is sequentially applied via the cuffs to the lower extremities of the patient synchronized by cardiac cycle. At early diastole, pressure is applied sequentially from the lower legs to the lower and upper thighs, to propel blood back to the heart. The procedure results in an increase in arterial blood pressure, retrograde aortic blood flow during diastole (diastolic augmentation), and systolic unloading, thus leads to enhanced flow perfusion not only to heart, but other ischemic organs, such as brain, kidney, eye, liver, etc. In 1976, a new external counterpulsation device applying pressure sequentially on the legs and thighs was successfully developed by Zheng and his colleagues in China and was further developed into enhanced external counterpulsation (EECP) in 1982. Since then, it has been extensively applied to clinical practice in China, and hundreds of reports have confirmed its safety and efficacy in coronary heart disease and other ischemic-related non-cardiac diseases. This article will review and discuss EECP applications in non-cardiac diseases involving brain, kidney, eye, and periphery.

Primary Hypertension
Huang studied 124 patients with systemic hypertension who underwent EECP, finding that EECP could significantly reduce the blood pressure in patients with mild or moderate hypertension. In their study, the systolic blood pressure decreased by 12.5% and diastolic pressure by 14.3% (P<0.01) after EECP for 1~2 treatment courses. In patients with normal blood pressure, however, there were no significant changes in blood pressure after EECP therapy (P>0.05). Mao and Yu also reported the antihypertensive effect of external counterpulsation. The mechanisms of antihypertension effect of external counterpulsation remain unclear. But external counterpulsation can improve venous return, increase the pressure of right atrium and stimulate the release of atrial natriuretic peptide, thus increase urinary sodium excretion and reduce plasma volume. External counterpulsation can increase renal blood flow, while increase urinary sodium excretion and reduce plasma volume as well.

Peripheral vascular disease
Animal experimental studies revealed that EECP did not cause peripheral vascular ischemia. On the contrary, EECP can improve the blood flow to distal extremities. Therefore it may play a role in the treatment of peripheral vascular diseases. Cai et al reported that 16 patients with lower limbs artery emphysema diseases (7 atherosclerosis obliterans, 9 buerger disease) were treated by EECP who were refractory to medical treatment. After EECP treatment, among 15 patients with pain of
the toe and/or heel, 14 cases' had pain relief or resolution; 10 intermission limp disappeared or relieved; 3 ulcer healed or decreased. The blood flow of lower limbs increased or achieved the normal range in 57% patients; and 80% patients' blood rheology was improved. Mo treated 52 patients with end-brush artery occlusion with PGEi and EECP. He allocated 52 patients into two groups randomly. One group was PGEi alone (20 patients), and the other received EECP plus PGEi (32 patients). The clinical effects were classified into five grades: significant improvement, improvement, slight improvement, no deterioration, deterioration. In the PGEi group, the results were 1, 5, 11, 2, and 1 respectively; in EECP plus PGEi group the results were 10, 12, 8, 2, and 0, respectively (p<0.05).

Neurological Diseases

1. Cerebrovascular ischemic diseases [6-9]

EECP has been applied into neurology department widely for cerebral infarction, cerebral thrombosis, lacunar infarct, transient ischemic attack, and vertebrobasilar ischemic. Yuan divided 44 patients with cerebrovascular ischemic diseases into two groups. One group was treated with medicine (red sage root, low molecular dextran and mannitol) and the other group was treated with EECP. They used 99m—Tc MIBI to measure the blood flow of cerebral pathologic area before and after the therapy for each group. If the blood flow increases by more than 15%, from 10% to 15%, from 5% to 10%, no more than 5%, it was called remarkable improvement, middle improvement, mild improvement, inefficacy, respectively. The results showed that in EECP group, ten patients got remarkable improvement, six got middle improvement, five mild improvement, and only one inefficacy. The total effective rate was 95%. But in medicine group, the results was three, five, three, eleven, respectively with a total effective rate of only 50% (P<0.001).

Yang treated 40 patients with acute cerebral infarction by EECP in comparison with other 40 patients treated by red sage root. The results indicated that the nerve function loss, TCD and local cerebral blood flow were improved significantly in the EECP group. There was a significant difference between the two groups. The improvement of nerve function was in relation to the increase of local blood flow. Liu divided 123 cerebral infarction patients into two groups randomly. One group was the EECP group, and the other group was a control. The results showed that the nerve function loss score of EECP group was much lower than that of control group (P<0.01), and the Fugl-Meyer motor function score of EECP group was much higher than that of control group (P<0.01). Tian treated 166 patients with cerebral infarction who were in convalescence phase by EECP for 2-3 treatment courses. He found that the total effective rate for nerve function loss was 95%. But in medicine group it was 90%. EECP has remarkable effects not only on acute and convalescent cerebral infarction but also on sequelae of cerebral infarction. Zhou reated 51 patients with vertebral artery type of cervical spondylosis by EECP. Patients’ clinical symptoms and vertebrobasilar ischemic were improved significantly in comparison with patients treated by medicine. Xing treated 34 patients with cerebral ischemic diseases by EECP for 1-4 treatment courses after 1~2 courses of medicine treatment. The result was satisfied and the total effective rate was 97%.

EECP can increase the blood flow of vertebral and cerebral arteries, which is proved by color Doppler ultrasound. Zhang reported that the blood flow in the vertebral artery of 94 patients with
vertebrobasilar ischemic increased 0.35 ml/s (16%) per stroke and the diastole peak velocity increased 0.14 ml/s (47%) after EECP. The blood flow of internal carotid artery increased 1.62 ml/s (26%). The blood flow of the two systems increased 3.94 ml/s. The author also found that the cerebral blood flow augment with the increase of the EECP treatment courses.

Yi allocated 45 patients with cerebral infarction into a routine medicine group (22 cases) and an EECP group (23 cases). EECP improved the hemodynamic parameters of the middle central artery, including peak velocity of blood flow (Vp), mean velocity of blood flow (Vm), Vp in diastole, and Vm in diastole. But in the routine medicine group, the improvements were not significant (P<0.01 compared to EECP).

Lv evaluated the long-term effects of EECP on TIA. They followed hospitalized patients with TIA from 1994 to 1998. There were 27 cases in the medicine group and twenty-eight in the EECP group. In the EECP group, 22 patients did not have a recurrence, 4 cases' attacks reduced remarkably, one patient died of myocardial infarction 23 months after discharge, and one had cerebral thrombosis 4 years after discharge. The total effective rate was 93%, and the full recovery rate was 79%. In the medicine group, 12 patients did not have a recurrence, 6 patients' attacks reduced remarkably, 3 patients unchanged, and 3 died of cerebral hemorrhage, myocardial infarction, cerebral thrombosis, respectively. And the total effective rate was 67% and full recovery rate was 44%. Lv suggested that if TIA lasted longer than 30 minutes, the patients should get 1~2 EECP treatment courses every other 1~2 months which can accelerate the control of TIA attack and decrease the full stroke rate and death rate.

2. Parkinson's disease (PD)[1011]

EECP can increase the cerebral blood flow which perhaps can improve the function of dopaminergic neurons, many neurotransmitters of brain stem and receptors. Liu divided 52 patients with PD into two groups: EECP and a, medical group treated with L-DOPA and Artane. The clinical effects were classified into five grades, including healed, remarkable improvement, improvement, mild improvement and inefficacy. The total effective rate of the EECP group was 92%, while in medicine group it was 81%. The rates of remarkable improvement of the EECP and medicine group were 73% and 43%, respectively. There was significant difference (P<0.01). Yang treated 30 PD patients with EECP for two treatment courses. The total improvement rate was 90%.

3. Alzheimer Disease (AD)[1215]

Up to the present, the particular pathogenesis of Alzheimer's dementia remains unclear. The cerebral blood flow of patients with Alzheimer's is reduced significantly and the metabolism of oxygen and glucose is reduced. Therefore, EECP may benefit the Alzheimer's patients by increasing the cerebral blood flow and the cerebral circulation and metabolism. Li treated 10 Alzheimer's patients with EECP. After 8 weeks, the cerebral blood flow increased significantly measured by SPECT. The activity of SOD and the content of dynorphin in blood rose. The concentration of growth hormone release is inhibited and the activity of SOD in cerebral spinal fluid increased remarkably. And the concentration of Pho and Met reduced. After EECP, the latent period of Ni wave of Alzheimer's patients' ERP shortened obviously and the occurring rate of P3 wave increased from 4 percent to 80 percent. Lin collected the information for three years from 49
Alzheimer's patients treated by EECP intermittently. He found that the cerebral circulation was improved significantly measured by SPECT. In addition, there were several clinical reports about the excellent effects through EECP combined with traditional Chinese herbs treatment.

**Sudden Deafness**

Sudden deafness is another disease whose pathogenesis remains unclear. No specific treatment have been identified. Many doctors consider the circulation disorder of the inner ear resulting from viral infection as the possible reason of the disease. EECP can increase the blood flow of common carotid artery, vertebrobasilar artery and their branches. Sequentially, the blood flow of cochlea increases. Then the blood and oxygen supply of cochlea are improved. All of the changes promote the improvement of audition. In 1986, Li, first reported the clinical effects of EECP on forty patients with sudden deafness. There have been more than 600 cases in China. Jiang treated 49 sudden deafness patients (51 ears) with EECP. The effective rate was 87%. And other 47 patients (49 ears) were treated with energy mixture and vasodilators. The effective rate was 65%. There was a significant difference between the two groups (P<0.01). In the study, they found if the courses of the diseases is shorter and the EECP treatment is performed earlier, the clinical effect will be more remarkable. On the contrary, if the courses of the disease is longer than 15 days, the clinical effect of the EECP treatment will be reduced.

Zhu and Zhou treated 126 sudden deafness patients with EECP and vasodilators. In the EECP group, the audition, the healed rate and the effective rate of deafness and tinnitus were all better than that of control group. Qu reported that they used high pressure oxygen and EECP to treat sudden deafness. The healed rate was higher than only using high pressure oxygen. Tang had the similar conclusion. Ren reported that if using Chinese herbs (Chuanxiong Qinand) EECP to treat sudden deafness, the therapy effect would be improved. In addition, Zhang studied the effect of the three therapy methods for sudden deafness, which were taking medicine, medicine and EECP, medicine and low energy He-Ne laser. They found that EECP could improve the microcirculation of the inner ear.

EECP should be performed immediately as soon as the diagnosis of sudden deafness is confirmed. During EECP therapy, vasodilator and microcirculation promoters may be continued.

**Retinopathy**

Many studies have indicated that EECP had improved some ischemic eyeground diseases, including central retinal artery thrombosis, ischemic optic nerve diseases, central serous chorioretinopathy, optic nerve atrophy and retinitis. Evaluating the clinical effect of EECP on ischemic eye diseases is easier and more confirmed than evaluating that of cardiac and cerebral ischemic diseases. After the EECP treatment courses, we can see the dilation of arteries and veins, dissolution and absorption of thrombus, and the improvement of pigmentation of optic disc by fluorescent light arteria retina angiography. In 1983, Pang reported that EECP is effective on treating central serous chorioretinopathy. Deng treated 85 central serous chorioretinopathy patients (88 eyes) with EECP. The results showed that 99% of patients’ eyesight and eyeground were improved, while in control group, only 70% of patients benefited (P<0.05). Liu treated 44 patients (54 eyes) with ischemic retinal diseases using EECP. After 1~3 treatment courses, eyesight and
eyegrounds of 49 eyes (94%) were improved, while 18 eyes (33%) eyesight and visual field recovered.

Yu performed EECP on 24 patients, including 5 central retinal artery block, 7 central retinal vein block, 5 optic nerve atrophy and 2 retrobulbar neuritis. After 1 treatment course, all of the eyes were improved except one with optic nerve atrophy. Chen treated 20 optic nerve atrophy patients (28 eyes) with EECP for 2~3 treatment courses. The eyesight of the 89% eyes was improved. Li treated 28 optic nerve atrophy patients (35 eyes) with EECP. The results showed that 14 patients (40%) had remarkable improvement, 12 (34%) got effective improvement, 5 (14%) improved, and 4 (11%) were ineffective. The total effective rate was 89%. Wang studied the changes of retinal oscillatory potential before and after the EECP. The results proved that 87% of the retinal vibration potential turned normal and the eyesight increased step by step after the therapy. The authors thought that EECP is a noninvasive, safe and effective way for ischemic optic nerve diseases, central retinal artery thrombosis and central retinal vein block. Retinal vibration potential test could be taken as an objective research method for evaluating the effect and prognosis of this kind of eye disease.

We must pay attention to the basic opinion that the increase of eye blood depends on the increase of the perfusion pressure. Therefore, the vasodilators and drug for improving metabolism have little effect. EECP is a promising to deal with this kind of disorders. On the other hand, the increase of eye blood flow can augment the intraocular dimension and the forming of aqueous humor. Thus, the intra-ocular pressure increases. Zheng treated 30 coronary heart disease patients without glaucoma and 3 glaucoma patients with EECP. He found that the intra-ocular pressure of patients without glaucoma didn’t change and the intra-ocular pressure of glaucoma patients increased remarkably. So the EECP treatment can be performed as long as the patients don’t have glaucoma.

Renal Insufficiency and Chronic Glomerulonephritis[3035]

EECP improves the blood flow of renal artery and maintains the renal perfusion pressure at a higher level. Shen measured (32 microglobulin pre- and post-EECP in serum and urine of 32 patients with COPD and renal damage by using radioimmunology. The results showed that after EECP, the concentration of [32 microglobulin in serum and urine were much lower than that before it (p<0.05; p<0.01, respectively), which indicated that EECP can improve the filtration and reabsorption of renal corpuscle. The next year, Xi studied the changes of RBC filtration index and the concentration of [32 renal corpuscl in serum and urine of 82 patients with coronary heart disease. They also found that EECP can not only enhance the transfiguration ability of RBC and improve the microcirculation and myocardial blood perfusion but also protect the function of kidney. Qian treated 35 chronic renal insufficiency patients with EECP. The average level of BUN and Cr were 23 mmol/l and 313 u.mol/l, respectively, before EECP. After the treatment, the average level decreased to 6.6 mmol/l and 130 umol/l, respectively (P<0.01). In addition, the 24-hour urine volume of the patients also increased.

In order to investigate the clinical effect of EECP on chronic glomerulonephritis Zhuang divided 96 patients into two groups, 60 in EECP groups and 36 in control group. In EECP group, the patients got 30 minutes treatment for one day and 15 days for a treatment period. Five days
after the first course, the second was performed. The results indicated that the clinical effective rate of EECP group was 78%, but only 50% in control group (P<0.05). There are three possible reasons for EECP improving renal function. First, EECP can increase the renal blood flow. Second, EECP can reduced the viscosity of plasma and blood. Third, EECP can improve renal microcirculation.

**Diabetes Mellitus (DM)**

Diabetes Mellitus (DM) is manifested by an elevated blood glucose level caused by the disorder of insulin secretion and utility. High blood sugar harms human vasculature and the damages are long-term and serious. If the situation lasts untreated, many organs and tissues can be involved, including eyes, heart, kidney, and peripheral vasculature. In 2002, Li reported the studies that 30 patients with DM treated by EECP. He estimated the concentration of blood sugar before and after the treatment of EECP. The results showed that after 2-4 treatment courses (one time daily, ten times a treatment course), 11 patients' blood sugar level reduced to normal, 16 to 7~9mmol/l, and 3 to 10~14mmol/l. After 4-6 treatment courses, all the patients' blood sugar became lower than 15mmol/l. The clinical practice indicated that EECP is an effective way to cure DM type II that gets poor response from long-term medicine.

Yao studied 60 patients with DM peripheral nerve lesion before and after the treatment of EECP. After EECP treatment, the pricking pain and neuralgia of 96 % patients disappeared; the abnormal sensation (sesame, chilly, heat, etc) of 91 % patients disappeared; The difficult ambulation of 56% patients was remarkably improved and the inflamed and the healing rate of wound was 67%. Electrophysiologic study showed that: the conduction velocity of peripheral nerve increased and the end-brush latent period shortened. Chen had the same conclusion.

Yao maintained that EECP can increase the blood flow of brain, upper abdomen, pancreas and spinal cord. The collateral circulation of endothelium base membrane of epineurium and the microcirculation of pancreas are improved. Thus the excretion of insulin increases, which can improve the metabolism of glucose and decrease the concentration of glucose, fructose and sorbitol in peripheral nerve. At the same time, the concentration of cyclohexanexhol increases. The swelling of nerve myelin sheath will be extinct. The breakage of myelin sheath can be plerosis. The kinesthetic perception of limbs and deep reflex are amelioration.

**Cerebral palsy**

In 1996, Wu reported that intracranial blood had low velocity and high resistance in cerebral palsy patients. She stated that besides the routine therapy, the methods that can improve the intracranial blood are important for the rehabilitation of cerebral palsy patients. From 1994 to 1998, Jiang measured the blood velocity and blood vessel resistance of 170 children with cerebral palsy patients. After 3 months' comprehensive therapy in which EECP was an important part, the intracranial blood velocity returned to normal. They selected 20 cases (12 males, 8 females) randomly, including 5 aged 0—12 months, 11 aged 13—36 months and 4 aged more than 36 months. Before and after the treatment, they measured the systolic velocity peak (Vpeak), mean blood velocity (Vmean), pulse index (PI) and resistance index (RI) of the middle cerebral artery
(MCA), anterior cerebral artery (ACA) and posterior cerebral artery (PCA), respectively. Before treatment, the Vpeak and Vmean of MCA and ACA were lower than normal, while after the treatment, all the data increased obviously. There was different significance between the two groups of data (P<0.01 or P<0.05). But the RI and PI of carotid artery decreased after the treatment. The two groups of sample were tested by t-test, and there was statistically difference (P<0.01 or P<0.05).

Jiang thought that EECP can improve the intracranial circulation and blood flow, which can benefit the functions of cerebral cells and promote the rehabilitation of patients with cerebral palsy.

Urolithiasis

Kuang studied the effects of EECP on treating renal calculi and renal colic in comparison with medical therapy. There were 89 patients in the EECP group and 37 in the medical group. In the EECP group, the patients received 30 minutes of treatment once or twice per day, and twelve times for one treatment course. The results showed that the stones of 73 patients (82%) were removed and all the patients' renal colic disappeared in EECP group while in the medicine group, the results were 1 patient and 8 patients, respectively. All the results proved that the effects of EECP treatment were better than that of medicine treatment. The author thought that after EECP, the renal blood flow and perfusion pressure increased which could raise the flow and velocity of aetiourine and accelerate the secretion of the renal tubule. All of the changes were important for the relief of renal colic and stone removal.

EECP therapy is the additional therapy of extracorporeal shock wave lithotripsy (ESWL). In the research, there were 17 patients still had 0.5cm stones after ESWL in the EECP group. The stones were removed after the EECP therapy. Clinical observations prove that EECP therapy is a simple, safe and effective method for renal and ureteral calculi that are smaller than 1 cm in diameter.

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