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Comparative Response of Oxidative Stress to Baduanjin Exercise Versus Electro-Acupuncture in Patients with Type 2 Diabetes Mellitus

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Abstract **Objective:** Oxidative stress is aggravated by the existence of type 2 diabetes mellitus. Baduanjin exercise and acupuncture are two traditional Chinese treatment methods that are commonly used to treat diabetes and its complications. This study aimed to compare the oxidative stress response to a 12-week electro-acupuncture versus Baduanjin exercise in patients with type 2 diabetes mellitus. **Material and Methods:** Sixty non-obese patients with type 2 diabetes mellitus were assigned randomly to the EA group (n=30) or Baduanjin-exercise group (n=30). EA group received a 2-Hz electro-stimulation to needles inserted in bilateral PC4 and PC6 acupoints for 40 minutes while the other group received Baduanjin exercise for 40 minutes. The 12-week treatment was performed daily (except Friday) in both groups. Besides the measurement of serum lipid hydro-peroxidase (as an oxidative stress marker), serum antioxidants such as superoxide dismutase and nitric oxide were assessed before and after 12 weeks. **Results:** Both EA and Baduanjin exercise produced a highly significant decrease in serum lipid hydro-peroxidase and an increase in serum superoxide dismutase and serum nitric oxide levels. Comparison of post-treatment lipid hydro-peroxidase, superoxide dismutase, and nitric oxide between Baduanjin exercise and electro-acupuncture

groups did not show a significant difference. **Conclusions:** Both Baduanjin exercise and electro-acupuncture are good anti-oxidative therapeutic modalities to lower oxidative stress in patients with type 2 diabetes mellitus.

Keywords Baduanjin Exercise, Electroacupuncture, Oxidative Stress, Type 2 Diabetes Mellitus, Elderly

1. Introduction

Type 2 diabetes mellitus (T2DM) is defined as a hyperglycemic disorder derived from weak secretion and/or action of insulin [1]. During diabetes mellitus, prolonged hyperglycemia is associated with the production of free radicals and the accumulation of oxidative stress (OS) leading to various T2DM-associated complications including cardiovascular diseases [2].

Oxidative stress is defined as the imbalance between the production of antioxidant enzymes and oxidative substances as reactive oxygen species (ROS) and reactive nitrogen species (RNS) (ROS and RNS are one-electron-free unpaired radicals with a highly toxic oxidative effect on the different cellular components). With the aging process, humans are vulnerable to the damaging effect of OS [3] which gives the start of pancreatic β-cell dysfunction that progresses to insulin resistance [4], then T2DM, diabetic micro-and macro-vascular complications [5].

Baduanjin exercise is an effective, feasible, non-drug, and cost-effective treatment option for T2DM, especially in older adults [6]. Baduanjin exercise is considered a moderate-intensity traditional Chinese exercise. This exercise is characterized by a series of smooth/continuous movements, whose performance demands position control, deep respiration, and coordination of the movements in different body parts (legs, arms, trunk, and head) to move from one position to another, moving the balance point without falling [7]. Baduanjin exercise can be used in the reduction of OS [8] and in the treatment of different T2DM-induced cardiovascular disorders such as dyslipidemia and hypertension [6].

Acupuncture, on the other side, is an old complementary treatment. This treatment - according to Chinese traditional medical theories - consists of strategic skin penetration at various points located on the body's particular meridians of energy (*qi*) flow. Electro-acupuncture (EA) (electrical stimulation through a needle inserted in the acupuncture points) [9] is considered a strong antioxidant therapeutic tool in rats with induced diabetes mellitus (DM) [10] or in subjects with obesity [11] and coronary heart disease [12]. Also, auricular acupuncture augmented the antioxidant system in high-risk subjects for DM [13]. Unfortunately, to our knowledge, no study compared the anti-oxidative effect of the bodily EA versus Baduanjin exercise, so this study was designed to deal with this comparison in T2DM patients.

2. Materials and Methods

2.1. Ethics

Besides the approval of the local ethical committee of Cairo University (P.T.REC/012/004211), declarative instructions of Helsinki were followed during the application of this prospective trial that was conducted from December 2022 to October 2024.

2.2. Criteria of Participants

Below a 30-kg/m^2 body-mass index (BMI), 60 elderly (from both sexes) with not-below five-year diabetic duration and ages > 65 years old were included.

The exclusion of high blood pressure, pulmonary, renal, cardiac, hepatic, and malignant disorders was confirmed. The researchers of this trial ruled out the patients who complained of arthritic articular problems of lower limbs. Also, the patients who received anti-oxidative supplemental agents, any type of complementary remedies, and sportive programs in the previous three months were ruled out.

2.3. Randomization

A randomized list - with two blocks - was constructed on a computer to assign the consented patients to two equal groups of number, EA (n=30) or Baduanjin exercise (n=30) groups (Figure 1).

2.4. EA Intervention

Bilateral PC4 and PC6 acupoints were selected for EA intervention in this study. The acupoints were located on the anterior surface of the forearm, 2 cun (for PC6) and 5 cun (for PC4) above the transverse crease of the wrist between the flexor carpi radialis and palmaris longus tendons [14]. The patients were rested in a supine position, then the PC4 and PC6 acupoints were swapped by a piece of cotton that was pre-soaked in seventy-percentage ethyl alcohol. Once the evoked *qi* sensation (tingling or numbness sensation in the punctured area) felt by every patient after inserting a sterilized needle (0.3x50 mm, Tony acupuncture needles, SUZHOU Medical Appliance, China) with a 0.5- to 1-cun perpendicular depth in every point, the tip of all needles was connected to a 2-Hz electrical current (668 Inter-TENS, made in Egypt). For 12 weeks, each EA session was applied daily – except Fridays –for 40 minutes.

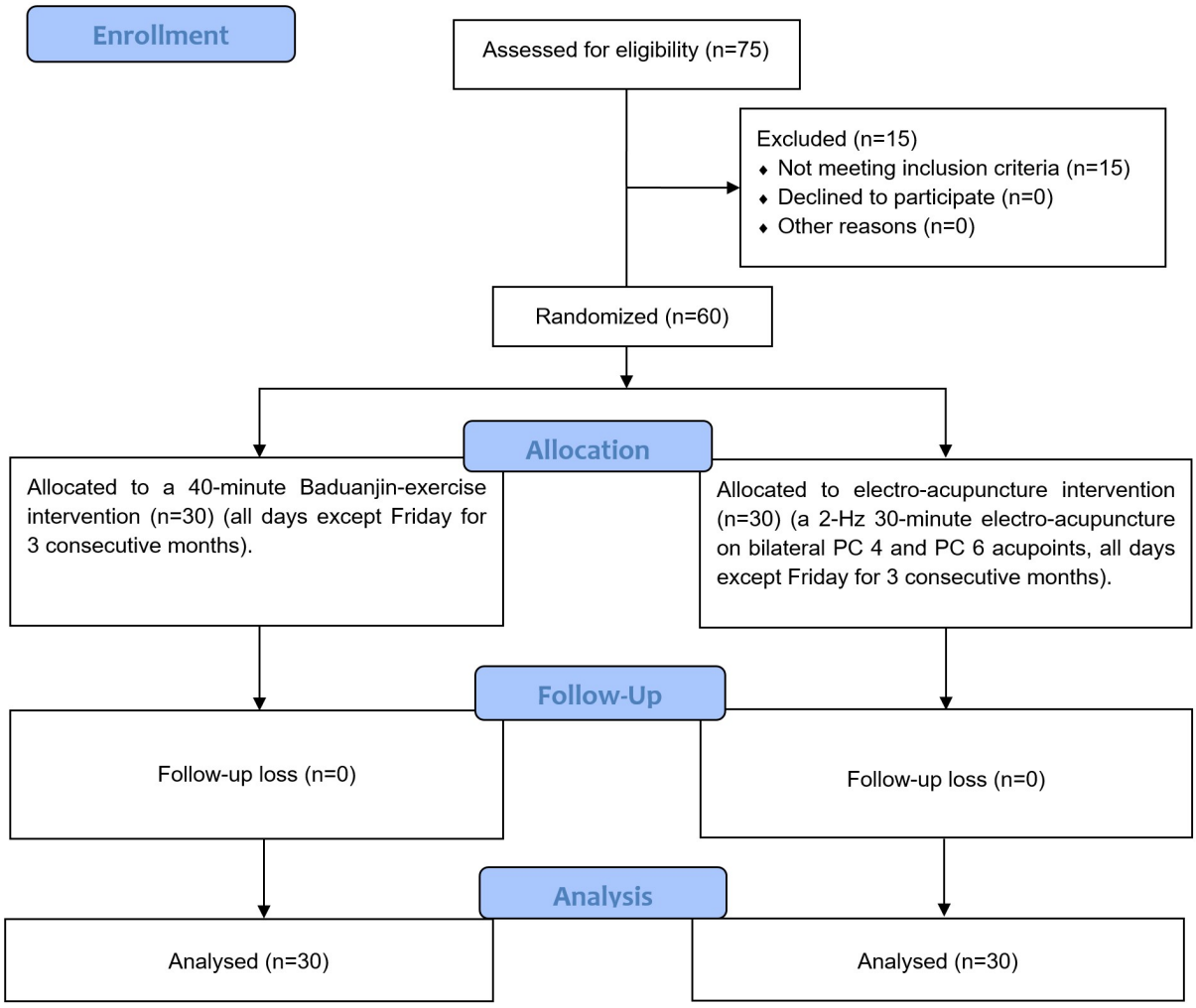

Figure 1. Trial consort flow

2.5. Baduanjin-Exercise Intervention

This interventional procedure, the Baduanjin exercise, originates from Health Qigong. According to the 2003 General Administration of Sport of China, the Baduanjin exercise consists of eight postural training. The first postural training: T2DM patients elevated their upper limbs upward with both palms facing the ceiling or the sky. The second postural training: T2DM patients posed as an archer to shoot left and right. The third postural training: T2DM patients elevated their right arm high and kept their left arm at the side of their body without movement, then elevated their left arm while keeping their right arm at the side of their body without movement. The fourth postural training: To look backward, T2DM patients turned their heads in full left and right directions from the standing position. The fifth postural training: T2DM patients turned their heads and buttocks. The sixth postural training: T2DM patients stooped and moved both hands to touch both feet. The seventh postural training: T2DM patients clenched fists and glared. The eighth postural training: T2DM patients raised and lowered their heels from standing position [15]. Every action within the posture was done for 5 min with a 40-min total time of session. For 12 weeks, each Baduanjin-exercise session was applied daily – except Fridays.

2.6. OS Assessment

Before and after 12 weeks, a 5-ml sample of venous blood was withdrawn to measure the serum lipid hydro-peroxidase (LOOH) (as a marker of oxidative stress), superoxide dismutase (SOD, as an antioxidant enzyme), and nitric oxide (NO) were measured in this comparative study.

The xanthine oxidase technique was used/utilized to evaluate SOD concentration/levels [16].

The NO levels in this comparative study were measured/evaluated in patients' plasma as nitrites utilizing the technique of modified Griess reaction after transferring the compounds of nitrates to nitrites compounds with vanadium chloride. Standard (ideal) curves for sodium nitrite were formed, then magnitudes of nitric oxide were reported [17].

Serum LOOH levels of this comparative trial in diabetic patients were measured/assessed with the orange assay of

ferrous ion oxidation–xylenol. The vital technique of this assay relies on the oxidative process of ferrous ionic compounds to ferric ions via various/different oxidants. The resultant ferric ionic compounds were assessed with xylenol orange. Levels of LOOH were detected from its reduction by the special reductant for lipids, triphenyl phosphine (TPP) [18].

2.7. Sample Size

Utilizing the T-test with a type II error equal to 80%, the sample size analysis (G*power, V.3.1.9.2, Germany) on 10 patients with T2DM revealed that the minimum number of the needed patients was 56 with an effect size of LOOH (as the main key parameter) = 0.76.

2.8. Statistical Analysis

The test of Kolmogorov-Smirnov confirmed the normality of all data. With a *P*-value, less than 0.05, version 18 of SPSS was used to analyze this comparative study's data. The analytic test, unpaired test, was used to assess the pretreatment between-group difference regarding demographic data (fasting blood glucose, BMI, and age). This test also was used to assess difference between groups' LOOH, SOD, and NO either pre or post treatments.

Chi-Square test assesses the pretreatment significance of sex distribution between the two studied groups.

Paired test was used to assess within- group significant changed values of LOOH, SOD, and NO at $P < 0.05$.

3. Results

3.1. Pretreatment Results

There was no pre-treatment significance of fasting blood glucose, BMI, and age between the EA and HIIET groups (Table 1). Also, there was no pre-treatment significance of LOOH, SOD, and NO between the two groups (Table 2).

Table 1. Demographic pre-treatment data of EA and Bad-ex groups

	EA group Mean ± SD	Bad-ex group Mean ± SD	P-value
Age (year)	68.86 ±3.51	68.20 ±3.14	0.445[a]
Sex*(F,M)	(14, 26)	(16, 24)	0.213[a]
BMI (kg/m^2)	27.00 ±1.56	27.76 ±1.52	0.06[a]
FBG (mg/dl)	166.10 ±29.97	165.60 ±29.35	0.948[a]

EA: Electro-acupuncture; **Bad-ex**: Baduanjin exercise; **SD**: Standard deviation; ***Chi-Square test, **F**: Female; **M**: Male; **Kg**: Kilogram, **m**: Meter; mg/dl: milligram/deciliter; **BMI**: Body mass index, **[a]**: Not significant, **FBG**: Fasting blood glucose.

3.2. Within-Group Comparison of Outcomes

The within-group comparison showed a statistical improvement in both groups' SOD, NO (the percentage of improvement in these two outcomes were high in EA group), and LOOH (the percentage of improvement in this outcome was high in Bad-ex group).

Also, the post-treatment comparison of SOD, NO, and LOOH between the two compared groups showed no significant changes/differences (Table 2).

Table 2. Analysis of OS in EA and Bad-ex groups

Parameter	**EA group**	**Bad-ex group**	**p-value**
SOD (NU/ml)	Mean ± SD	Mean ± SD	
Pre	62.33 ±24.77	61.80 ±23.60	0.932[a]
post	244.66 ±92.02	211.33 ±85.94	0.564[a]
P-value within the group	< 0.001[b]	< 0.0001[b]	-
Percentage of improvement	↑292.52%	↑243.575	-
NO (µmol/L)	Mean ± SD	Mean ± SD	
Pre	376.16 ±180.27	378.16 ±181.33	0.966[a]
Post	484.23 ±199.28	474.23 ±205.88	0.849[a]
P-value within the group	0.003[b]	0.008[b]	-
Percentage of improvement	↑28.72%	↑25.405%	-
LOOH (µmol/L)	Mean ± SD	Mean ± SD	
Pre	0.78 ±0.37	0.81 ±0.36	0.728[a]
Post	0.65 ±0.40	0.48 ±0.28	0.078[a]
P-value within the group	0.035[b]	< 0.001[b]	-
Percentage of improvement	↓16.66%	↓40.74%	-

OS: Oxidative stress; **EA**: Electro-acupuncture; **Bad-ex**: Baduanjin exercise; **SD**: Standard deviation, **mmHg**: Millimeter mercury; **SOD**: Superoxide dismutase; **µmol/L**: Micromole per liter; **NO**: Nitric oxide; **NU/ml**: Nano-enzyme unit per milliliter; **LOOH**; Lipid hydro-peroxide; **[a]**: No significance difference, **[b]**: Significance difference.

4. Discussion

The evidence-based antioxidant mechanism of EA is not obvious and is less discussed in the literature [19], especially with the very limited studies on risky individuals for cardiovascular diseases.

The cause of improved OS after a 12-week EA may be related to the decrease in OS markers, increased action of anti-oxidant enzymes, and diminished production of ROS. ROS-inhibited production after EA is induced by the inhibited expression of pro-oxidants, modulated molecular pathways related to the signaling of ROS generation, and enhanced respiratory mitochondrial functions that stimulate the mitophagy removal (mitophagy removal is described as the indirect and selective removal of ROS by autophagy mechanism of mitochondria) [20].

Neuronal nitric oxide synthase (nNOS) and inducible nitric oxide synthase (iNOS) - with the assistance of tetrahydrobiopterin (BH4) – are the main key enzymes that convert L-arginine to L-citrulline to produce NO [21]. Increased production of antioxidants such as NO is exerted by the EA-inducing expression of nNOS and iNOS in rats with hypercholesterolemia [22], lipopolysaccharide-induced kidney injury [23], acetylsalicylic acid-induced acute gastritis [24], and spontaneous hypertension [25].

In rats with induced different conditions such as Parkinson's disease [26,27], postoperative-induced cognitive dysfunction [28], and spinal cord injuries [29], EA increased the levels of SOD due to the reduced levels of systemic inflammatory markers. Also, in rats with streptozotocin-induced hyperglycemia [30,31] or polycystic ovary syndrome (PCOS) [32], increased antioxidant levels (SOD) may be related to the positive effect of EA on OS, hypoglycemia, and hyperinsulinemia. Suppressed production of the mediators involved in the process of OS such as nicotinamide adenine dinucleotide phosphate (NAPDH) oxidase is thought to be responsible for attenuating the diabetic-induced ischemic injury to the cerebral tissues after EA [33].

Approving the results of this study, the alleviated OS injury in addition to increased SOD is the cause of maintained reperfusion to ischemic myocardial tissue after bilateral PC6 EA in patients with valve replacement [34]. Also, a low-calorie diet with EA is highly effective in improving OS in obese subjects [11]. Twenty-day auricular acupressure increased the concentration of antioxidant enzymes (SOD) in the high risky persons for DM [13]. As indicated by SOD increase, two acupuncture courses separated with 1- to 1.5-month rest (each course constituted from 9 to 11 sessions) are considered a good antioxidant therapy in patients with the bronchopulmonary, peripheral nervous system, gynecological, or locomotor pathologies [35].

Physical activity is a vital factor affecting OS and oxidative DNA destruction since a sharp elevation in during-exercise oxygen consumption leads to an elevation in ROS production. To be noted, the effect of exercise-induced oxidative DNA destruction is a variable depending on the parameters of exercise prescription (type, mode, duration, and intensity of exercise). One session of exercise increases OS and oxidative DNA destruction; on the other side, regular moderate-intensity exercise sessions decrease them. Under the basic concept of hormesis, low-to-moderate production of ROS which is evoked by regular moderate-intensity physical activity is beneficial, since it activates the gene expression of transcription proteins. These proteins stimulate the production of key anti-oxidative enzymes [36]. Since Baduanjin exercise is considered a moderate-intensity exercise, regular performance of this exercise can regulate and/or increase the antioxidants and decrease the occurrence of oxidative stress [8]. Also, due to the improved psychological stress, autonomic nervous system dysfunction, cardiovascular risk factors, endothelial dysfunction, and cortisol and melatonin production, the regular performance of mediation and repeated slow breathing during Qigong exercise are associated with better antioxidant activities [37].

Very limited studies investigated the effect of the Baduanjin exercise on OS. Only one study published in 2008 investigated this effect on OS in middle-aged women. The results of the study of 2008 reported that a 12-week Baduanjin exercise had a significantly increasing effect on SOD and a lowering effect on malondialdehyde (MDA) (a marker for OS) in middle-aged women [8]. Considering Baduanjin exercise falls under the umbrella of Qigong Chines rehabilitation (slow body movements with breathing exercises), an 8-week Qigong training in young sedentary females significantly increased their serum antioxidants (total antioxidant capacity and catalase enzyme) and decreased their serum MDA [38]. A 12-week T'ai chi exercise - as a subtype of Qigong training - produced a significant improvement in MDAs levels of T2DM patients [39]. Also, a significant increase in total antioxidant capacity and a decrease in the oxidative stress score after a 6-month T'ai chi exercise in the metabolic-syndrome elderly were documented [40].

Regulated metabolic and cardiovascular functions augmented by the 12-week exercise-imposed vascular shear stress may be the cause of a significant increase in NO and SOD in T2DM patients [41]. The elevated production of NO synthase may be the cause of increased NO in the soleus muscle of rats after a ten-week treadmill training [42].

Despite the non-significant increase of NO in the 12-week EA group or the 12-week aerobic-exercise group (opposite to the results of this study), SOD significantly increased in both groups and LOOH showed a significant decrease in the aerobic exercise group only in patients with coronary artery disease [12]. Also, a 14-session EA did not improve SOD in rats with simulated weightlessness [43]. Opposite to the results of this study, a 6-week follow-up after a 15-week course of aquatic-based exercise and manual acupuncture showed significantly declined SOD in diabetic patients [44]. Despite the significant increase in

NO, SOD was not elevated after the program of 12-week aerobic exercise in T2DM patients [45]. Low levels of circulating l-arginine may be the cause of not increased levels of NO after aerobic exercise for 16 weeks in diabetic patients [46].

4.1. Study Limitations

The absence of a post-study follow-up to the results of EA or Baduanjin exercise was the main limitation of this trial.

5. Conclusions

Both Baduanjin exercise and EA are good anti-oxidative therapeutic modalities to lower the OS in patients with T2DM. This study ensures that string role of complementary therapies, exercise or acupuncture, in controlling diabetes mellitus-induced oxidative stress.

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Conflict of Interest

The authors of this EA-vs-exercise trial conducted on sixty older patients with T2DM conducted report no conflict of interest.

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