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Original Article

Effect of Wet Cupping versus Moderate Intensity Aerobic Exercise on Inflammatory Markers in Diabetic Patients

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Abstract:

Background/Objectives: This study was conducted to investigate the effect of wet cupping therapy versus moderate-intensity aerobic exercise on inflammatory markers in diabetic patients. **Methods:** Sixty diabetic males were selected from Deraya University Physical Therapy Center in Minya to participate in this study from March to August 2024. Their ages varied between 30 and 50 years. The individual was randomly assigned to two groups. Group A were treated with wet cupping therapy once per month for 2 months, and Group B were treated with aerobic exercises that involve walking on a treadmill machine, three sessions/week, for eight weeks. Serum interleukin 6 as well as tumor necrosis factor-alpha (TNF-α) levels were assessed prior to and following treatment for each group. **Results:** The study's findings revealed a substantial reduction in serum interleukin 6 as well as (TNF-α) following treatment in both groups (p-value < 0.001). There was a substantial difference between both groups following treatment regarding interleukin 6 (95% CI where p-value < 0.001), as well as TNF-α (95% CI where p-value = 0.001) in favor of group A. **Conclusions:** It can be concluded that wet cupping is an effective adjuvant therapy in decreasing inflammatory markers in diabetic patients more than moderate-intensity aerobic exercises.

Keywords: Wet cupping, Aerobic exercises, Interleukin 6, Tumor necrosis factor-alpha (TNF-α).

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1. Introduction

TNF-α, in conjunction with TNFR-1, is crucial in activating and attracting immune cells to amplify inflammation. TNF-α promotes transcriptional pathways that elicit oxidative stress, which then interacts with inflammation to facilitate cellular degeneration [1]. The pro-inflammatory actions of TNF-α include the production of prostaglandins and the activation of COX-2. Prostaglandins are regarded as pro-inflammatory agents in chronic inflammatory responses. Reports indicate that TNF-α activates inflammatory cells as well as begins inflammatory cascades inside arterial walls [2].

Among the pro-inflammatory indicators, TNF-α was initially identified as a contributor to the etiology of insulin resistance along with glucose-related disorders associated with T2DM [3]. One of the hallmarks of type 2 diabetes is insulin resistance, the phenomenon whereby cells fail to react to normal amounts of insulin. TNF-α is an important factor in insulin resistance development because it decreases the expression of GLUT4, an insulin-regulated glucose transporter mostly found in adipocytes, skeletal muscles, as well as cardiac muscles [4]. TNF-α is crucial in the pathogenesis of insulin resistance, particularly in males with a higher body mass index relative to females [5].

It has been reported that adding TNF-α to experimental animal models or cell cultures improves insulin action compared to models without TNF-α or its receptors, suggesting that TNF-α plays a role in the development of insulin resistance [6].

Chronic inflammation, characterized by increased interleukin 6 (IL-6) levels, is linked to diabetes, cardiovascular disease, chronic kidney disease, as well as conditions such as nonalcoholic fatty liver disease. Elevated IL-6 levels may result from excess adipose tissue that can induce aberrant glucose metabolism, potentially leading to diabetes as well as various manifestations of glucotoxicity in multiple tissues and organs, including the vasculature, heart, kidneys, as well as liver. IL-6 is linked to atherosclerosis, cardiovascular disease, as well as chronic renal disease. The illustration is neither comprehensive nor complex [7].

By regulating cell differentiation, migration, proliferation, as well as apoptosis, the proinflammatory cytokine IL-6 leads to inflammation and ultimately insulin resistance along with the pathophysiology of T2DM. Although IL-6 is naturally present in tissues, prolonged exposure to it and irregular synthesis can cause inflammation, which in turn can cause insulin resistance and overt type 2 diabetes. A mechanistic link exists between IL-6 stimulation as well as insulin resistance. IL-6 induces insulin resistance by hindering the phosphorylation of the insulin receptor as well as insulin receptor substrate-1 through the upregulation of suppressor of cytokine signaling 3 (SOCS-3), a possible inhibitor of insulin signaling. This article succinctly outlines the mechanism by which IL-6 develops insulin resistance and the pathophysiology of T2DM. Inhibiting IL-6 and its signaling pathways may serve as an effective approach for preventing inflammatory disorders associated with insulin resistance as well as T2DM [8].

Cupping therapy is a conventional treatment that employs a bamboo or glass cup to generate suction on the skin over a painful region or acupuncture point [9]. Cupping is an Islamic therapeutic method employed in numerous nations globally [10]. Cupping therapy is categorized as dry and moist cupping. Wet cupping enhances blood circulation and stimulates the autonomic nervous system [11].

Both approaches employ containers constructed from diverse materials to establish a vacuum over a designated area of the skin. In a wet cupping procedure, suction is employed to extract small volumes of blood as well as extracellular fluid from the body, usually following the creation of minor incisions or superficial skin abrasions, and normally in much lesser quantities than traditional bloodletting methods [12].

Dry cupping is thought to promote lymphatic uptake by increasing oncotic pressure, which in turn helps the treated area rid itself of excess fluids and waste [12]. In wet cupping, the incisions created using a scalpel during the process result in a distinct array of results. These small skin incisions promote the migration of inflammatory cells and initiate the release of endogenous opioids, which are natural compounds that serve as analgesics as well as mood enhancers. This activity enhances both innate as well as acquired immunity, thereby improving the body's capacity to combat infections along with restore immunological balance [13].

Aerobic exercise, sometimes referred to as endurance activities, cardio, or cardio-respiratory exercise, is physical activity of varying intensity that primarily relies on the aerobic energy-generating mechanism. "Aerobic" means "relating to, involving, or requiring oxygen" and describes the process of using oxygen to sufficiently meet energy demands during endurance exercise through aerobic metabolism. Aerobic exercise is the continuous repetition of light to moderate intensity activities over prolonged durations. Examples of cardiovascular or aerobic exercise include medium- to long-distance running or jogging, swimming, cycling, stair climbing, as well as walking [14].

2. Materials and Methods

Subjects:

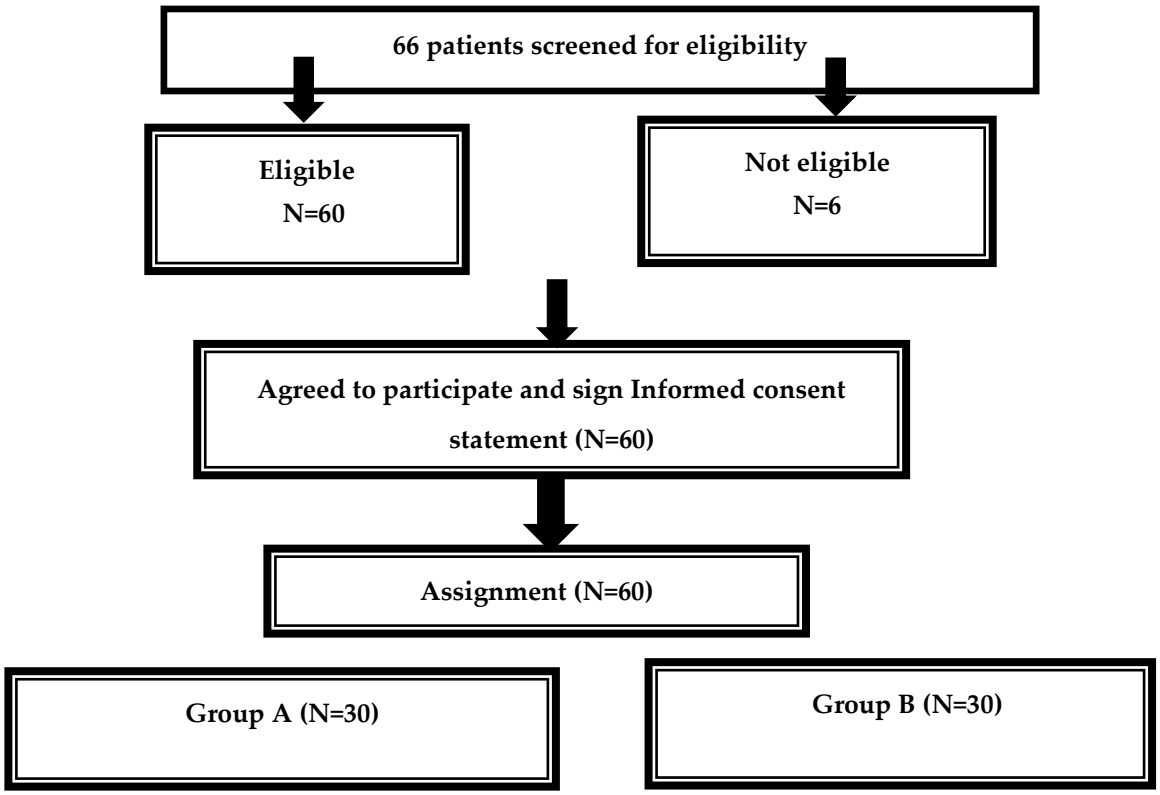
Sixty diabetic males participated in this study. They were selected from Deraya University, Faculty of Physical Therapy, Minya, Egypt from March 2024 to August 2024. There aged between 30 and 50 years were recruited from the outpatient clinic of Deraya University. All participants had diabetes for over 10 years, with a BMI ranging from 25 to

29.9 kg/m². All patients were administered an oral hypoglycemic medication. Patients with hepatic diseases, cancer, renal failure, orthopedic issues or extremity fractures, hypertension, and neurological disorders e.g., hemiplegia, Parkinsonism, and epilepsy were excluded from this study.

The research obtained approval from the Ethical Committee of the Faculty of Physical Therapy at Cairo University (P.T. REC/012/005160). and also, Clinical Trials.gov (NCT06667648) was recorded first registration at 16/10/2024.

Design of this study:

Design of this study was randomized controlled study. The enrolled patients were randomly assigned to two distinct groups after finishing the consent form. Group A were treated with wet cupping therapy once per month for 2 months, and Group B were treated with aerobic exercises that involve walking on a treadmill machine, three sessions/week, for eight weeks.



Flow Chart

Assessment

Body mass index was determined for both groups prior to the commencement of the investigation using the Model MC. Health scale RTZ-120A, manufactured in China. Blood sample kits were used to detect serum IL-6, TNF-α, as well as blood sugar levels prior to and following treatment in both groups. Pulse oximeter to measure pulse rate during exercise session.

Procedures:

Patients in group (A) received medication and wet cupping therapy once per month for 2 months. Each cupping session lasted approximately 30 to 40 minutes and could be executed in five phases. The initial phase involved primary suction. In this phase, the therapist allocated specific points or areas for cupping then disinfected the area, which was located at the upper back (opposite to C7), paraspinal, and below the scapula. After placing appropriately sized cups on the chosen locations, air was removed from the cups manually. The cups were left in place for three to five minutes. The second step was puncturing with a needle to get blood out from the body to inside the applied cups. In the third step, suction and bloodletting were performed, allowing blood to accumulate inside the cups for 3 to 5 minutes. The negative pressure in the cups was then released through the valve, and the cups were emptied of the accumulated

blood. Afterward, the cups were reapplied to the skin using the same procedure for an additional 3 to 5 minutes. Following the removal of the cup in the fourth step, the fifth step involved dressing the area after it had been cleaned and disinfected with an FDA-approved skin disinfectant [15].

Patients in group (B) receive medication and aerobic exercise as the following:

1. The training procedures were elucidated for each subject.
2. All subjects in the study (group A) attended the program of walking on a treadmill machine for eight weeks in accordance with the subsequent parameters: -

- Mode of exercise: aerobic exercise.
- Intensity: according to heart rate 60-75% (maximum heart rate - resting HR) + resting HR

Max.HR = 220 - age. & resting HR is the number of heartbeats during rest [16].

Heart rate: determined by sensor of treadmill and/or pulse oximeter.

- Duration: 30 to 40 minutes every session. Each session comprised 5-10 minutes of warm-up exercises on a treadmill at a constant speed and intensity, followed by an equivalent cooling-down phase. The conditioning exercise lasted 20 minutes, featuring an increase in treadmill speed to achieve 60-75% of the MHR.
- Frequency: 3 times/week for 8 weeks [17].

Statistical analysis

An unpaired t-test was conducted for the comparison of subject characteristics between groups. The data was examined for normal distribution using the Shapiro-Wilk test. To ensure homogeneity across groups, we used Levene's test for variance homogeneity. When comparing IL-6, TNF-α, and postprandial blood glucose levels between groups, an unpaired t-test was used. When comparing pre- and post-treatment levels, a paired t-test was employed. All statistical tests were set to have a significance level of $p < 0.05$. Statistical analysis was carried out using SPSS version 25 for Windows, a program developed by IBM SPSS in Chicago, IL, USA.

3. Results

Subject characteristics:

Table 1 presents the characteristics of subjects in Group A and Group B. No substantial differences were observed between the groups regarding age, weight, height, as well as BMI ($p > 0.05$).

Table 1. Comparison of subject characteristics between Group (A) and Group (B):

	Group(A)	Group(B)		
	Mean ±SD*	**Mean ±SD**	**t- value**	**p-value***
Age (years)	52.30 ± 5.76	51.90 ± 6.72	0.20	0.48
Weight (kg)	73.50 ± 5.84	75.25 ± 4.93	-1.02	0.31
Height (cm)	169.70 ± 3.37	168 ± 4.27	1.39	0.17
BMI (kg/m²)	25.58 ± 2.61	26.75 ± 2.62	-1.41	0.16

* SD, Standard deviation; MD, Mean difference; p-value, Probability value

Statistical analysis serum interleukin 6, tumor necrosis factor-alpha, and postprandial blood glucose:

Within group comparison, there was a substantial reduction in serum IL-6, TNF-α, as well as postprandial blood glucose following treatment in both groups contrasted with prior to treatment ($p > 0.001$). The percent of change in serum IL-6, TNF-α, as well as postprandial blood glucose of Group (A) were 64.41, 68.11, and 37.88%, and that in Group (B) were 48.51, 52.42, and 34.31%. **(Table 2).**

Between-group comparison, there was no substantial difference among groups prior to treatment ($p > 0.05$). Comparison among groups following treatment revealed a substantial reduction in serum IL-6, TNF-α, as well as postprandial blood glucose of Group (A) contrasted with that of Group (B) ($p < 0.05$).

Table 2. Mean serum interleukin 6, tumor necrosis factor-alpha, and postprandial blood glucose pre- and post-treatment of Group (A) and Group (B):

	Pre-treatment	Post-treatment				
	Mean ±SD*	**Mean ±SD***	**MD***	**% of change**	**t- value**	**p-value**
Serum interleukin 6						
Group (A)	83.25 ± 26.26	29.63 ± 12.51	53.62	64.41	16.21	0.001
Group (B)	82.05 ± 23.46	42.25 ± 14.59	39.8	48.51	12.41	0.001
MD	1.2	-12.62				
t- value	0.15	-2.93				
	p = 0.88	p = 0.006				
Tumor necrosis factor-alpha						
Group (A)	84.50 ± 19.98	26.95 ± 9.84	57.55	68.11	21.09	0.001
Group (B)	82.70 ± 24.87	39.35 ± 10.65	43.35	52.42	11.66	0.001
MD	1.8	-12.4				
t- value	0.25	-3.83				
	p = 0.80	p = 0.0٠1				
Postprandial blood glucose (mg/dl)						
Group (A)	302.80 ± 14.86	188.10 ± 10.57	114.7	37.88	38.40	0.001
Group (B)	299.30 ± 16.01	196.60 ± 11.64	102.7	34.31	34.38	0.001
MD	3.5	-8.5				
t- value	0.71	-2.44				
	p = 0.47	p = 0.02				

*SD, Standard deviation; MD, Mean difference; p-value, Probability value

4. Discussion

This study was designed to find out the impact of wet cupping versus moderate-intensity aerobic exercise on inflammatory markers among diabetic patients. Our statistical analysis revealed no significant difference in age as well as BMI among the two groups at baseline, indicating that both groups were comparable regarding these variables. The results revealed that both moderate-intensity aerobic exercise and wet cupping improved IL-6, TNF-α among diabetic patients following 8 weeks in favor of wet cupping. The percentage of improvement was -64.41% in Group (A), while it was -48.51% in Group (B) for serum interleukin 6, and -68.11% in Group (A) while -52.42% in Group (B) for serum tumor necrosis factor-alpha.

This finding indicates that cupping may contribute to inflammation reduction, since the cupped regions of blood vessels can increase the release of nitric oxide from endothelial cells, thereby diminishing inflammation through improved blood flow to the tissues of the body.

Previous research indicated that cupping therapy is linked to a decrease in the release of proinflammatory markers like TNF-α as well as IL-6 (Abbasi and Najafi, 2023) [18].

This aligns with the findings of (Marziyeh et al. 2017) [19}, who corroborated the results of this study, indicating that after the 12-week intervention, participants in the aerobic groups experienced an increase of over 20% in TNF-α levels. They demonstrated that TNF-α is a cytokine mostly produced by monocytes and macrophages infiltrating adipose tissue. Nonetheless, other immune cells, including lymphocytes as well as natural killer cells, may also synthesize it. Elevated levels of TNF-α are typically linked to cellular apoptosis, cardiovascular disorders, and inflammatory responses.

Conversely, Gultai et al. (2011) [20] conducted a study in which they compared the impacts of three distinct exercise modalities—aerobic training, resistance training, as well as combined (aerobic along with resistance training)—on

metabolic control, insulin resistance, inflammatory markers, adipocytokines, as well as tissue expression of insulin receptor substrate-1 (IRS-1) following 12 weeks of training. The patients in the study were 48 with T2DM. No substantial differences in TNF-α level were seen following 12 weeks of aerobic training.

Mihriban Arslan et al. (2014) [21] contradicted our finding as they approved that, Following the exercise training program, there was no change in the levels of TNF-α, and no association was discovered between TNF-α and either mass drug administration (MDA) or waist circumference. One possible explanation for this disparity is that the current study used a smaller sample size. Consequently, it is necessary to do more extensive and varied research to evaluate how exercise training affects TNF-α levels and how they relate to MDA and waist circumference. Our findings indicate that individuals with T2DM mellitus should be promoted to enhance their physical activity levels in order to prevent the early onset of chronic diseases associated with diabetes mellitus.

5. Conclusions

It can be concluded that wet cupping is an effective adjuvant therapy in decreasing inflammatory markers in diabetic patients more than moderate-intensity aerobic exercises.

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Conflict of Interest: The author declares no conflict of interest.

Ethical committee: The research obtained approval from the Ethical Committee of the Faculty of Physical Therapy at Cairo University (P.T. REC/012/005160).

Clinical trials: Clinical Trials.gov (NCT06667648) was recorded first registration at 16/10/2024.

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