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Original Article

EFFECTS OF APPLE CIDER VINEGAR ON VEGF165 AND GLUCOSE LEVEL IN DIABETIC MELLITUS TYPE-II PATIENTS

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ABSTRACT:
The purpose of this clinical trial was to evaluate the effect of apple cider vinegar on VEGF165 and glucose levels in type-II diabetes Mellitus (DM) patients. A randomized clinical trial using a non-probability convenience sampling technique was conducted on 110 eligible types-II diabetes Mellitus patients who failed to control their glucose levels and were scheduled for senile cataract surgery. Participants were given15-20 ml of apple cider vinegar in 200 ml water before sleep at night for 6 months (with follow-up after each 3 months). HbA1C, Fasting Blood Sugar, and VEGF165 tests were performed Pre and Post operatively and analysed using SPSS version 21. A total 110 type-II diabetic patients with NPDR in both eyes were included. The highest proportion of patient was in the age group of 51-60 years (54.4%), females were 61.5% and majority were illiterate about (37.2%). About 58.2% patients strictly followed their medication, about 53.1% patients strictly followed their diet plane and about 48.2% patients strictly took apple cider vinegar daily. Significant mean changes were found in VEGF165 ($p<0.002$), HbA1C ($p<0.023$), and blood sugar fasting ($p<0.012$). Regular use of apple cider vinegar was effective in controlling diabetes and reducing the abnormal production of VEGF165 (retinal protein) in type-II DM patients and it helped improve ocular condition allowing ophthalmologist to perform cataract surgery more easily and remove the dense cataract.

KEYWORDS: Apple Cidar Vinegar, Diabetes type II, Randomized controlled trial (RCT)

INTRODUCTION

Diabetes mellitus (DM) commonly known as diabetes, is a group of metabolic disorders characterized by a high blood sugar levels over a prolonged period of time (1). Diabetes is due to either when the pancreas does not produce enough insulin, or when the cells of the body do not respond properly to the insulin produced (2).

Type 2 diabetes begins with insulin resistance, a condition in which cells fail to respond to insulin properly. As the disease progresses, a lack of insulin may also develop. This form was previously referred to as non-insulin-dependent diabetes mellitus (NIDDM) or adult-onset diabetes. The most common cause is a combination of excessive body weight and insufficient exercise (3). As of 2019, an estimated 463 million people had diabetes worldwide (8.8% of the adult population), with type 2 diabetes making up about 90% of the cases (4). Rates are similar in women and men. And trends suggest that rates will continue to rise (5).

In 2021, diabetes was the direct cause of 1.6 million deaths and 47% of all deaths due to diabetes occurred before the age of 70 years. Another 530 000 kidney disease deaths were caused by diabetes, and high blood glucose causes around 11% of cardiovascular deaths (6). The primary complications of diabetes due to damage in small blood vessels including damage to the eyes, kidneys, and nerves. Damage to the eyes, known as diabetic retinopathy, is caused by damage to the blood vessels in the retina, and can result in gradual vision loss and eventual blindness(7). The platelet-derived growth factor (PDGF) family includes VEGF. VEGF-A, VEGF-B, VEGF-C, VEGF-D, and placental growth factor, which are located on chromosome 6p12, make up the VEGF gene family (8). VEGF plays a crucial role in angiogenesis by binding to its receptors, which promotes the formation of new blood vessels and the proliferation of endothelial cells. A cascade of receptor activation is necessary for the complex and well-coordinated process of new vessel formation and development. VEGF is a crucial rate-limiting step in physiological angiogenesis (9). The deletion of a single VEGF allele, which results in poor vascularization, has highlighted the crucial role that VEGF plays in angiogenesis. VEGF121, VEGF145, VEGF148, VEGF162, VEGF165, VEGF165b, VEGF183, VEGF189, and VEGF206 are the nine isoforms of VEGF-A (10). VEGF165 is the most prevalent isoform in the eye (11). Cells

in the body produce a protein called vascular endothelial growth factor (VEGF). When the body needs new blood vessels, VEGF stimulates their formation. However, cells can sometimes produce too much VEGF, which leads to abnormal blood vessels formation in the eye. These abnormal blood vessels impair vision and can damage the eye.
The causes and origins of age-related eye illnesses are multifactorial and complex. Oxidative stress has been identified as a common contributing factor because the eye has high oxygen consumption, high levels of polyunsaturated fatty acids, and cumulative exposure to high-energy visible light, making it vulnerable to oxidative stress. Antioxidants may help maintain vision or even reverse visual damage, according to some theories. Therefore, the role of dietary antioxidants and the possible therapeutic benefits of antioxidant supplements as an easy and affordable method of disease prevention and control are of great research interest (12).
Apple cider vinegar is produced apple juice, through fermentation. During fermentation, yeast convert the alcohol into acetic acid. To avoid issues such as tooth enamel erosion, 1 to 2 tablespoons (15–20 ml) should be diluted in water or tea before consumption (13).
Consuming apple vinegar may help people with diabetes and dyslipidaemia improve their glycaemic control and reduce oxidative stress, according to a 2019 clinical trial. A review of research trials conducted in 2021 also suggested that glycemic status may improve with ACV consumption. Apple cider vinegar has been investigated in recent years as a potential weight loss, heart health, and even dandruff treatment (14).
Drinking vinegar may help combat obesity, according to research from Japanese scientists. According to one tiny study, vinegar helped a group of individuals with type 2 diabetes with their insulin and blood sugar levels (15).
Consuming large amounts of apple cider vinegar can have negative effects on the stomach, throat, and teeth due to its strong acidity. Additionally, it may reduce the effectiveness of some medications, including drugs for heart disease and diabetes, as well as laxatives and diuretics (16).

METHODS

The Randomized Clinical Trial (RCT) was conducted in accordance with the term of Helsinki Declaration and also was approved by the institutional Research and Ethical Committee.
A total 110 patients with Non-Proliferative Diabetic Retinopathy (NPDR) and types-II Diabetic Mellitus were included in the study. There was no gender restriction, and patients aged between 40 to 70 years were included in the study. A non-probability convenience sampling technique used. Patients were included in the study if they were diagnosed with type-II diabetes mellitus and had non-proliferative diabetic retinopathy (NPDR) in both eyes. Only patients aged between 40-70 years were eligible for inclusion. Additionally, patients with a history of diabetes mellitus were included in the study. All participants who were willing to use apple cider vinegar regularly and provided written informed consent were included in the study. Patients were excluded from the study if they were younger than 40 years or older than 70 years of age. Patients with a history of diabetes mellitus for less than five years were also excluded. Individuals with other types of diabetes mellitus such as type I diabetes or gestational diabetes, were not included in the study. Patients suffering from other systemic diseases that could affect the study outcomes were excluded. Furthermore, patients with proliferative diabetic retinopathy (PDR) in one or both eyes were excluded from the study. The study was performed according to a protocol approved by the hospital's Institutional Ethics Committee, in accordance to the ethical principles of the Helsinki Declaration and written informed consent (English and Urdu) was obtained from each patient. A preliminary screening test was done, including history of diabetes, blood sugar level, type of diabetes, Patients were educated about the about apple cider vinegar, its benefits, method of use and recommended daily quantity.
Collection of aqueous humor samples was performed in the operating theatre under sterile conditions on first visit without using apple cider vinegar and after using (3 months and 6 months). Samples (0.1 – 0.2 ml) of aqueous humor were collected in sterile tubes by way of limbal anterior chamber puncture with a 27-gauge needle of a 1-ml insulin injector. These samples were then stored frozen at –80°C within a few minutes of collection.
The concentration of the VEGF165 isoform was measured by enzyme-linked immunosorbent assay (ELISA) with human VEGF kit (Invitrogen U.S.A.-BioSource Human VEGF Immunoassay kit Catalog # KHG0112 / KHG0111). The linear detection range of the assay was 5–1500 pg/ml.
Data were analysed using SPSS version 21. Descriptive data were presented as frequencies and percentages. One-way ANOVA was used to compare the group means. Pearson correlation analysis was used to measure the strength of the relationship between the variables. The 95% confidence intervals of the tests were determined; $P < 0.05$ was accepted as statistically significant.

RESULTS

Among the patients, 48.2% strictly used apple cider vinegar, 36.4% used it moderately, and 25.4% used it irregularly (Table 1). The results are summarized and analysis of the groups was done by using the ANOVA-One way test. However, VEGF165, HbA1C and Blood Sugar Fasting significantly changed after using apple cider vinegar for 3 months and 6 months.

Aqueous VEGF165 before intervention (BI) Mean ± S.D was 320.6 ± 239.3 pg/ml, after intervention (AI) Mean ± S.D was 242 ± 72.5 pg/ml on 3 months and 133.3 ± 58.5 pg/ml on 6 months. (Table 2).

HbA1C before intervention (BI) Mean ± S.D was 9.32 ± 1.74, after intervention (AI) Mean ± S.D was 8.65 ± 1.81 on 3 months and 8.08 ± 1.36 SD on 6 months. (Table 3).

Blood Sugar Fasting before intervention (BI) Mean ± S.D was 170.14 ± 62.42, after intervention (AI) Mean ± S.D was 157.34 ± 58.16 on 3 months 133.2 ± 58.16 on 6months. (Table 4).

The Mean ± S.D value of Aqueous VEGF165 (Vascular Endothelial Growth Factor) was 242 ± 72.5 pg/ml, Blood Sugar Fasting was 157.34 ± 58.16 and HbA1C was 8.65 ± 1.81 on first follow-up (3 months) and 133.3 ± 58.5 pg/mlof VEGF165, Blood Sugar Fasting was 133.2 ± 58.16 and HbA1C was 8.08 ± 1.36 on second follow-up (6 months).(Table 5).

Table 1: Distribution of patients using apple cider vinegar

	Characteristics	Percent
Apple cider vinegar follow-up	Strictly follow	48.2%
	Moderately follow	36.4%
	Irregular	25.4%
	Total	**110**

Table 2: Effects of Apple cider vinegar on VEGF 165 at 3 months and 6 months

Apple Cider Vinegar	Aqueous $VEGF_{165}$ (Mean ± S.D)	P-value
Before Intervention	320.6 ± 239.3 pg/ml	
First follow up (3-months)	242 ± 72.5 pg/ml	**0.002**
Second follow up (6-months)	133.3 ± 58.5 pg/ml	

Table 3: Effects of Apple cider vinegar on HbA1C at 3 months and 6 months

Apple Cider Vinegar	HbA1C (Mean ± S.D)	P-value
Before Intervention	9.32 ± 1.74	
First follow up (3-months)	8.65 ± 1.81	**0.023**
Second follow up (6-months)	8.08 ± 1.36	

Table 4: Effects of Apple cider vinegar on Blood Sugar Fasting at 3 months and 6 months

Apple Cider Vinegar	Blood Sugar Fasting (Mean ± S.D)	P-value
Before Intervention	170.14 ± 62.42	
First follow up (3-months)	157.34 ± 58.16	**0.012**
Second follow up (6-months)	133.2 ± 58.16	

Table 5: Effects of Apple cider vinegar on VEGF 165, Blood Sugar Fasting & HbA1C at 3 months and 6 months

After using apple cider vinegar		
Clinical tests	First follow-up at 3 months (Mean ± S.D)	Second follow-up at 6 months (Mean ± S.D)
Aqueous $VEGF_{165}$	242 ± 72.5 pg/ml	133.3 ± 58.5 pg/ml
Blood Sugar Fasting	157.34 ± 58.16	133.2 ± 58.16
HbA1C	8.65 ± 1.81	8.08 ± 1.36

DISCUSSION

In current study VEGF165 were significantly reduced on both follow-up periods (3 months and 6 months ($p<0.002$) in patients with diabetic retinopathy. Previous studies support the generally accepted assumption that the VEGF165 level in the aqueous humor collected from the anterior chamber adequately reflects the VEGF165 activity in retinal tissues, despite a lower level of VEGF165 levels compared to the vitreous humor (17). Based on these clinical data, we investigated the relationship between the severity of diabetic retinopathy and VEGF165 level through aqueous humor sampling.

In our study, the aqueous VEGF165 levels observed in type-II diabetic patients with NPDR were consistent with results of the previous studies regarding the role of VEGF165 in retinopathy (severity to generate new vessels in retina of eye). A correlation between elevated VEGF165 in ocular fluids and the presence of retinopathy has been revealed by some clinical studies, suggesting that VEGF165 is a mediator for hypoxic inflammation (18).

The aqueous levels of VEGF165 were elevated in eyes and were also correlated with the severity of diabetic retinopathy. There was a statistically significant difference between aqueous VEGF165 levels in after intervention in patients with type-II diabetes mellitus.

In the current study, HbA1C and blood sugar fasting were significantly reduced HbA1C ($p<0.023$), blood sugar fasting ($p<0.012$). Previous study results showed HbA1C ($p=0.002$) and blood sugar fasting ($p=0.006$) significantly reduced in the intervention group but not significantly changed in these parameters of the placebo group (19). Another study showed a significant reduction in fasting blood sugar ($p=0.05$), in vinegar (750 mg) ingestion group when compared with vinegar pills (40 mg acetic acid) as control group after 12 weeks trail but no significant change in Hb1C and post prandial glucose was found (20).

In the current study, diet remained the same, no significant difference was found in any dietary component before and after the intervention. Previous study human studies also reported that diet should remain the same before and after the acetic acid intervention in type-II diabetic patients to ensure comparability (21).

A study conducted on human subjects also showed physical activities and life style remained the same before and after the invention and no significant effect of these confounders was found.

Apple cider vinegar was most effective in controlling diabetes and reducing the abnormal production of VEGF165 (retinal protein) in type-II diabetes mellitus patients, thereby helping to control the progression of the eye complications. Furthermore, improved ocular conditions may facilitate ophthalmologists in performing cataract surgery more easily and removing dense cataract.

Conflict of Interest

Authors declare no conflict of interest.

Ethical consideration

The study was approved by Institutional Research Ethics Committee.

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REFERENCE

1. "About diabetes". World Health Organization. Archived from the original on 31 March 2014. Retrieved 4 April 2014
2. Shoback DG, Gardner D, eds. (2011). "Chapter 17". Greenspan's basic & clinical endocrinology (9th ed.). New York: McGraw-Hill Medical. ISBN 978-0-07-162243-1
3. RSSDI textbook of diabetes mellitus (Revised 2nd ed.). Jaypee Brothers Medical Publishers. 2012. p. 235. ISBN 978-93-5025-489-9. Archived from the original on 14 October 2015.
4. "IDF DIABETES ATLAS Ninth Edition 2019" (PDF). www.diabetesatlas.org. Retrieved 18 May 2020.
5. Vos T, Flaxman AD, Naghavi M, Lozano R, Michaud C, Ezzati M, et al. (December 2012). "Years lived with disability (YLDs) for 1160 sequelae of 289 diseases and injuries 1990–2010: a systematic analysis for the Global Burden of Disease Study 2010". Lancet. 380 (9859): 2163–96. doi:10.1016/S0140-6736(12)61729-2
6. Global Burden of Disease Collaborative Network. Global Burden of Disease Study 2021. Results. Institute for Health Metrics and Evaluation. 2024
7. "Diabetes Program me". World Health Organization. Archived from the original on 26 April 2014. Retrieved 22 April 2014.
8. Pasqualetti G, Danesi R, Del Tacca M, Bocci G. Vascular endothelial growth factor pharmacogenetics: a new perspective for anti-angiogenic therapy. Pharmacogenomics. 2007;8(1):49-66
9. Yancopoulos GD, Davis S, Gale NW, Rudge JS, Wiegand SJ, Holash J. Vascular-specific growth factors and blood vessel formation. Nature. 2000;407(6801):242-8.
10. Bhisitkul RB. Vascular endothelial growth factor biology: clinical implications for ocular treatments. Br J Ophthalmol. 2006;90(12):1542-7.
11. Soker S, Takashima S, Miao HQ, Neufeld G, Klagsbrun M. Neuropilin-1 is expressed by endothelial and tumor cells as an isoform-specific receptor for vascular endothelial growth factor. Cell. 1998;92(6):735-45
12. Li C., Miao X., Li F., et al. Oxidative stress-related mechanisms and antioxidant therapy in diabetic retinopathy. Oxidative Medicine and Cellular Longevity. 2017; 2017:15. doi: 10.1155/2017/9702820.9702820
13. University of Washington, The Whole U: “Beyond the Hype: Apple Cider Vinegar as an Alternative Therapy.”
14. Bioscience, Biotechnology and Biochemistry: “Vinegar intake reduces body weight, body fat mass, and serum triglyceride levels in obese Japanese subjects.
15. Journal of Diabetes Research: "Vinegar Consumption Increases Insulin-Stimulated Glucose Uptake by the Forearm Muscle in Humans with Type 2 Diabetes.”
16. Annals of Cardiology and Angiology: “Anti-obesogenic effect of apple cider vinegar in rats subjected to a high fat diet.”
17. Qaum T, Xu Q, Joussen AM, Clemens MW, Qin W, Miyamoto K, et al. VEGF-initiated blood-retinal barrier breakdown in early diabetes. Invest Ophthalmol Vis Sci. 2001; 42:2408–13.

18. Funatsu H, Yamashita H, Nakamura S, Mimura T, Eguchi S, Noma H, et al. Vitreous levels of pigment epithelium-derived factor and vascular endothelial growth factor are related to diabetic macular edema. Ophthalmology. 2006; 113:294–301. doi: 10.1016/j.ophtha.2005.10.030.
19. Mahmoodi, Mehdi, et al. "The effect of white vinegar on some blood biochemical factors in type 2 diabetic patients." Journal of Diabetes and Endocrinology, Vol. 4, No. 1, 2013, pp. 1-5.
20. Johnston, Carol S., Samantha Quagliano, and Serena White. "Vinegar ingestion at mealtime reduced fasting blood glucose concentrations in healthy adults at risk for type 2 diabetes." Journal of Functional Foods, Vol. 5, No. 4, 2013, pp. 2007-11.
21. Mitrou, P., et al. "The role of acetic acid on glucose uptake and blood flow rates in the skeletal muscle in humans with impaired glucose tolerance." European Journal of Clinical Nutrition, Vol. 69, No. 6, 2015, p. 734.