TRADITIONAL AND INTEGRATIVE MEDICINE

Trad Integr Med, Volume 4, Issue 3, Summer 2019

Original Research

Novel Thermal-Therapy Protocol (SINA1.2) from Traditional Persian Medicine (TPM): A Pilot on Diabetic Rats

Zahra Sarbaz Hoseini[1], Majid Asghari[1], Hamid Heidari[2] Abolfazl Mohammadbeigi[3], Mahdi Alizadeh Vaghasloo[4]*

[1]*School of Traditional Persian Medicine, Qom University of Medical Sciences, Qom, Iran*
[2]*School of Medicine, Qom University of Medical Sciences, Qom, Iran*
[3]*Department of Epidemiology and Biostatistics, School of Health, Qom University of Medical Sciences, Qom, Iran*
[4]*Department of Traditional Medicine, School of Persian Medicine, Tehran University of Medical Sciences, Tehran, Iran*

Received: 13 Jul 2019 **Accepted:** 23 Jul 2019

Abstract

One of guilty pathologies in insulin resistance and type 2 diabetes mellitus (T2DM) is ectopic fat accumulation in organs like pancreas, liver and skeletal muscles due to fatty acid's bad digestion. This situation corresponds much with a spectrum of illnesses named the *Soo ul Qinya & Estesgha* in Traditional Persian Medicine (TPM). We renamed and redefined the concept as "*The Bad-Anbaasht Syndrome*" meaning bad-deposition. One of its basic treatments mentioned is thermal-therapy which interestingly also shown to benefit T2DM in recent studies. We designed a novel protocol named SINA therapy to treat T2DM including sauna's benefits but reducing its side effects and then performed an animal pilot study. Five Wistar rats made diabetic by high fat diet and low dose streptozotocin, were treated daily by month long SINA 1.2 treatment protocol (1 cc Oxymel gavage and then 30 min thermal therapy in 37℃ dry sauna incubator). Weight and blood glucose were measured at beginning and at the end. Although Mean weights increased significantly from 296 to 321 (paired T test, $p = 0.022$) but surprisingly the mean blood glucose lowered significantly from 200mg/dl to 127mg/dl ($p = 0.049$). According to results of this pilot study, SINA therapy 1.2 is probable to have benefits in treatment of T2DM, but yet needs further experimental and clinical evidence.

Keywords: Diabetes; Insulin resistance; Persian medicine; Thermal-therapy; SINA therapy

Citation: Sarbaz Hoseini Z, Asghari M, Heidari H, Mohammadbeigi A, Alizadeh Vaghasloo M. **Novel Thermal-Therapy Protocol (SINA1.2) from Traditional Persian Medicine (TPM): A Pilot on Diabetic Rats.** Trad Integr Med 2019; 4(3): 102-108.

*Corresponding Author: Mahdi Alizadeh Vaghasloo
Department of Traditional Medicine, School of Persian Medicine, Tehran University of Medical Sciences, Tehran, Iran
Tel: +98 21 8899 0837
Email: mhdalizadeh@gmail.com

Introduction

Diabetes mellitus is a global common metabolic disorder that affected approximately 425 million people by 2017 [1]. The incidence of the disease has increased dramatically and has caused more than 3 million deaths in 2012 worldwide [2]. It is also predicted to be the seventh cause of death in the world by 2030 [3]. According to World Health Organization (WHO) reports, this disorder affects 10% of the Iranian population and accounts for 2% of mortality at the national level [4]. It is the largest cause of blindness, kidney failure, heart attack, and lower-extremity amputation in the world, which demonstrates the importance of treating and preventing diabetes complications [2].

The role of ectopic fat storage has been pointed out in pathological investigations on insulin resistance and type 2 diabetes [5,6,7]. Fat can be recognized as food as it is a source of energy storage, a member of the cell structure, and a part of the intracellular and intercellular messaging system [8]. Normally, the body consumes and stores fatty acids through reactions, but sometimes these processes can be impaired for a variety of reasons, including excessive fat consumption. Excessive fatty acids enter the systemic circulation due to different issues and in addition to causing disorders in whole body, enter tissues that are unable to consume and store them and thus are stored improperly. This ectopic accumulation reduces tissue integrity and induces pathological responses and structural and functional damage in all cells [8,9].

Ectopic fat storage occurs in many tissues and causes various complications. The most important of these citations include the heart, liver, skeletal muscles, pancreas, and kidneys [10]. Ectopic cardiac fat accumulation occurs in the pericardium, epicardium, myocardium, and around the coronaries which leads to impaired cardiac rhythm, muscle function and blood perfusion [8,11,12,13].

The same problem causes insulin resistance in the skeletal muscles and leads to the production of inflammatory cytokines and oxidative stress mediators, changes in lipid profile and insulin resistance in the liver. Ectopic fat accumulation in the pancreas causes disorders, the most important of which includes pancreatic β-cell dysfunction [14,15,16]. Overall, lipids can become key components of the pathophysiological cascade that are detrimental to cell health and tissue function. They may also impose adverse effects such as impaired intracellular components, chronic inflammation and impairment of energy, metabolism and vital responses and finally cell death. This indicates the need of attention to such an issue in the treatment of diabetes and its complications.

In this study, in harmony with recent global approach and WHO recommendations towards integrative medicine [17], we reviewed Traditional Persian Medicine (TPM/PM) literature to find a solution for ectopic fat storage.

In a quest in PM works, two topics were identified as the nearest concepts to ectopic fat storage named *Soo ul Qinya & Estesgha*

(S&E) سوءالقنیه و استسقاء, which listed a range of ectopic and harmful storage of food in the body [18,19,20]. S&E seem to be a spectrum of a diseases that starts from poor hepatic digestion and then progresses to poor vascular and organ digestion [21]. This poor digestion, for whatever reason, results in uncompleted rheological change called "*Nozj*" and subsequently impure blood production [22]. Furthermore, circulating throughout the body and penetrating into different organs, bad-digested food gradually accumulates in organs ectopically as it is unusable by them. Then again, due to subsequent lack of blood supply and deprivation of "*intrinsic fuel*" named "*Haar-re-Gharizi*" [23], the organ cannot digest and expel these wastes, resulting in weakness and disintegrity of the body organs [19,24,25].

Although *S&E* has been defined only based on macroscopic indices, we have adopted and abstracted from it, a more general and common concept named "*The Bad-anbaasht syndrome*" [23,26,27] which means ectopic and harmful food storage in the body in different scales ranging from nanoscopic to macroscopic levels. One of the displays of this syndrome is the ectopic fat storage in different body tissues which may have diverse manifestations depending on the individuals' condition and the organs affected.

Considering the similarities between *S&E* and ectopic fat storage, the treatments were sought for the disease from the traditional manuscripts. Generally, such treatments can be obtained firstly by deducing from general principles given in the opening chapters and secondly referring to traditional prescriptions provided by the previous scholars under specific topics and disorders in the following chapters.

Regarding general principles of Persian Medicine (PM), the governing nature of the body is the one who fights disease and separates good humor from harmful ones and excretes the harmful humors and wastes [19]. In these processes, the "*intrinsic fuel*"-mainly comparable with the whole blood - strengthens the nature of the body and acts as its arm or device to do the above and to preserves body moistures at a healthy level, and prevents them from being harmful and pathogenic [23,25]. According to the literature, heart is the source and pump of the "*intrinsic fuel*" which moves and distributes it in the whole body [23,27]; therefore, strengthening the heart enhances the "*intrinsic fuel*" and its distribution throughout the body and to the surface and helps modify the body as the scholars have regarded the "*intrinsic fuel*" as the source of all functions. This point of view nowadays is more understandable because whole blood is now known to contain a range of nutrition and defense capabilities to fulfill cell and tissue requirements and also the medium conveying warmth and wetness which are two qualities that boosts development and growth when adequate. In PM literature, moderate but not excessive external heat has been considered generally to empower the heart and thus to expand the "*intrinsic fuel*" and subsequently inflame the in-

nate heat. Therefore, by better distribution of "*intrinsic fuel*" (whole blood) to the peripheral organs that are away from the heart, not only their temperament [28] will be adjusted, but also their digestive, excretory, functional, and defensive abilities are also promoted to an optimal level. It is notable that migrating to warmer climates or using warm baths has also been specially recommended in *S&E* treatment sections [29].

It is noteworthy that thermal therapy is also one of the most effective methods currently available as diabetes adjuvant therapy in conventional medicine. It has been shown to significantly decrease insulin resistance, fasting blood glucose, and glycosylated hemoglobin in diabetic samples in numerous recent animal and human studies [30,31,32,33]. It is also shown to control inflammatory reactions [32] and to improve the quality of life for patients with type 2 diabetes [34]. Numerous articles have addressed the role of thermal therapy in reducing complications and contributing to the recovery of diabetic patients [32,35,36]. Mechanisms currently presented for these achievements include increased production and induction of nitric oxide synthase (NOs) as well as induction of heat shock protein (HSP) [31,37,38,39]. Although positive inotropic and chronotropic effects of heat on the heart and vasodilation effect on the arteries should also be considered as it helps better end organ perfusion and food-drug bioavailability [23,40].

On the other hand, blood and fluid thinning syrups like oxymel [41] – a finely baked sugar and vinegar mixture – have been generally and also specifically prescribed for such conditions. Oxymel disintegrates thick, aggregated materials including blood constituents and intercellular and intracellular depositions providing a more fluid medium for transportation of nutrients, mediators and drugs thus better tissue bioavailability and reduction of insulin resistance. Oxymel consumption has not shown increasing effect on fasting blood sugar (FBS) of normal people [42].

Besides thermal therapy and oxymel consumption derived and deduced from the general principles of PM, some specific treatments and medications have also been discussed under the *S&E* topics including the use of topical ointments such as combinations of chamomile, salt, borax and cow fat (tallow) in order to prepare and induce suitable sweating from the skin to expel the accumulated waste dermally [29,43] although such treatments are not applicable in experimental rats due to the covered skin and lack of peripheral sweat glands [44]

According to the foregoing, we composed a treatment protocol (SINA1.2) [23] for type 2 diabetic rats by combining warm oxymel gavage with subsequent controlled comfortable thermal-therapy. This method was designed and implemented as a pilot study.

Methods

Animals

In this study, five male Wistar rats (4 weeks old) weighing 150-200 g were obtained from

Pasteur Institute. The rats were exposed to 12 hours of light and 12 hours of darkness at 22 ± 1 °C. Rats had free access to water and food (normal or high fat).

Maintenance protocols and animal experiments were carried out according to the ethics committee of the Qom University of Medical Sciences. (Ethical code: IR.MUQ.REC.1396.15)

Diabetes Induction

Rats were fed a high-fat diet for 8 weeks, then, after 12 h fasting, a single dose of citrate buffer-dissolved streptozotocin (25 mg/kg) was injected intraperitoneally [45]. Rats with fasting blood sugar (FBS) levels of above 150 mg/dl after the third day were included in the study.

Treatment

The treatment was performed for 4 weeks in a way that rats were gavaged with oxymel five days a week and then placed in a dry-warm sauna chamber at 37 °C for 30 minutes. This protocol was named SINA1.2 method.

Simple oxymel syrup preparation

One kg of sugar was boiled with 500 ml of warm water, then 300 g vinegar (5% acetic acid) was added and slightly stirred and boiled again.

For gavage, 0.2 cc of oxymel syrup was mixed with 0.8 cc of water which reached its boiling point temperature (100 °C), then cooled to 50 °C.

The rats' weight and FBS were measured at 10-day intervals. FBS was measured by a glucometer using the tail blood of the animal.

Findings

Rats' weight ranged from an average of 296 g on the first day to 321 g on the last day, which was shown significantly increased by paired t-test (P = 0.022). However, interestingly, despite weight gain, the mean FBS decreased from 200 mg/dl at baseline to 127 mg/dl at the end of the study, which was statistically significant (P = 0.049).

Discussion and Conclusion

As mentioned previously, from modern physiology point of view, the external heat increases the peripheral vasodilatation to modulate the increased core body temperature; therefore the heart is forced to increase its output by increasing the stroke volume and pulse rate to maintain the intra-arterial pressure. This respectively increase in inotropy and chronotropy half an hour a day for about a month seems to increase left ventricular hypertrophy and heart's pumping ability, thus resulting better blood supply to the liver, pancreas, other tissues, and removal of more fats and decrease in insulin resistance. In regards to oxymel, interestingly, four weeks of intake not only did not elevate FBS levels in diabetic rats but also along with controlled thermal therapy (sauna) - in the SINA1.2 protocol – it reduced the FBS. This result may be related to the blood thinning and tissue cleansing effect claimed for oxymel which might have increased insulin bioavailability and decreased insulin resistance. Another remark-

able point was the opposite change in weight and FBS levels which may be related to a probable porosity and swelling temporarily made by oxymel's effect on the fat depositions which may have substituted water instead of fat in the short term. This probability is also compatible with the possible increased insulin access and bioavailability.

Further studies should consider lipid profiles as well as inflammatory factors that cause diabetes complications. It is also recommended to investigate changes in various tissue in future histopathological studies.

Conflicts of Interest

None.

Acknowledgments

None.

References

[1] Cho NH, Shaw JE, Karuranga S, Huang Y, da Rocha Fernandes JD, Ohlrogge AW, Malanda B. IDF Diabetes Atlas: Global estimates of diabetes prevalence for 2017 and projections for 2045. Diabetes Res Clin Pract 2018;138:271-281.

[2] Global report on diabetes World Health Organization Geneva, 2016.

[3] Mathers CD, Loncar D. Projections of global mortality and burden of disease from 2002 to 2030. Plos med 2006;3:e442.

[4] World Health Organization-Diabetes, country profiles 2016. Available from: http://www.who.int.

[5] Borén J, Taskinen MR, Olofsson SO, Levin M. Ectopic lipid storage and insulin resistance: a harmful relationship. J Intern Med 2013;274:25-40.

[6] Gustafson B, Hedjazifar S, Gogg S, Hammarstedt A, Smith U. Insulin resistance and impaired adipogenesis. Trends Endocrinol Metab 2015;26:193-200

[7] Samuel VT, Shulman GI. The pathogenesis of insulin resistance: integrating signaling pathways and substrate flux. J Clin Invest 2016;126:12.

[8] Ertunc ME, Hotamisligil GS. Lipid signaling and lipotoxicity in metabolic inflammation: indications for metabolic disease pathogenesis and treatment. J Lipid Res 2016:jlr.R066514.

[9] Lim S, Meigs JB. Links between ectopic fat and vascular disease in humans. Arterioscler Thromb Vasc Biol 2014;34:1820-1826.

[10] Rosen ED, Spiegelman BM. What we talk about when we talk about fat. Cell 2014;156:20-44.

[11] Goldberg IJ, Trent CM, Schulze PC. Lipid metabolism and toxicity in the heart. Cell Metab 2012;15:805-812.

[12] Han TS, Lean MEJ. A clinical perspective of obesity, metabolic syndrome and cardiovascular disease. JRSM Cardiovasc Dis 2016;5:2048004016633371.

[13] Ruiz-Núñez B, Dijck-Brouwer DJ, Muskiet FA. The relation of saturated fatty acids with low-grade inflammation and cardiovascular disease. J Nutr Biochem 2016;36:1-20.

[14] Byrne CD, Targher G. Ectopic Fat, Insulin Resistance, and Nonalcoholic Fatty Liver Disease. Implications for Cardiovascular Disease 2014;34:1155-1161.

[15] Lyons C, Kennedy E, Roche H. Metabolic Inflammation-Differential Modulation by Dietary Constituents. Nutrients 2016;8:247.

[16] Samuel VT, Shulman GI. Mechanisms for insulin resistance: common threads and missing links. Cell 2012;148:852-871.

[17] Organization WH. WHO traditional medicine strategy 2014–2023. 2013. Geneva: World Health Organization. 2015.

[18] Heravi M. Bahr al-Jawaher. Jalaluddin Publications. Qom 2008; p 22. [in Arabic]

[19] Kermani N. Sharh al-Asbab va al-Alamat. Vol 1. Jalaleddin. Qom 2008; p 34. [in Arabic]

[20] Pourhosseini M, Nojavan F, Mohammadbeigi A, Moradi H. Misinterpret of a unique clinical presentation named "Soo ul qinya" in Traditional Persian medicine with "Anemia". IJAM 2019; 10:130-135.

[21] Emtiazy M, Keshavarz M, Khodadoost M, Kamalinejad M, Gooshahgir SA, Shahrad Bajestani H, Relation between body humors and hypercholesterolemia: An Iranian traditional medicine perspective based on the teaching of Avicenna. Iran Red Crescent Med J 2012;14:133-8.

[22] Alizadeh Vaghasloo M, Zareian MA, Soroushzadeh SMA. The Concept of Nozj. Trad Integr Med 2016;1:133-135.

[23] Alizadeh Vaghasloo M, Naghizadeh A. The Concept of the Haar-re-Gharizi and Hararate Gharizi: The Innate Hot [Substance] and Heat. Trad Integr Med 2017;2:3-8.

[24] Jorjani L. Zakhireh kharazmshahi. Bonyade Farhang Ira. Tehean 1992; p 653.

[25] Ibn Sina A. al-Qanun fi al-tibb. Alamy Le-Al-Matbooat institute. Lebanon 2005; pp 125-127.

[26] Alizadeh Vaghasloo M, Naghizadeh A, Keshavarz M. The Concept of Pulse. Trad Integr Med 2017;2:54-60.

[27] Moradi F, Alizadeh F, Naghizadeh A, Karimi M, Alizadeh Vaghasloo M. The Concept of "Masam" (Pores) in of Persian Medicine. Trad Integr Med 2017;2:160-165.
[28] Shirbeigi L, Zarei A, Naghizadeh A, Alizadeh Vaghasloo M. The Concept of Temperaments in Traditional Persian Medicine. Trad Integr Med 2017;2:143-156.
[29] Nazem Jahan MA. Exireh Azam. Vol 3. Iran University of Medical Sciences & Health Services Research Institute for Islamic and Complementary Medicine (RICM). Tehran 2008; p 66. [In Persian]
[30] Geiger PC, Gupte AA. Heat shock proteins are important mediators of skeletal muscle insulin sensitivity. Exerc Sport Sci Rev 2011;39:34.
[31] Henstridge DC, Whitham M, Febbraio MA. Chaperoning to the metabolic party: the emerging therapeutic role of heat-shock proteins in obesity and type 2 diabetes. Mol Metab 2014;3:781-793.
[32] Krause M, Ludwig MS, Heck TG, Takahashi HK. Heat shock proteins and heat therapy for type 2 diabetes: pros and cons. Curr Opin Clin Nutr Metab Care 2015;18:374-380.
[33] McCarty MF, Barroso-Aranda J, Contreras F. Regular thermal therapy may promote insulin sensitivity while boosting expression of endothelial nitric oxide synthase–effects comparable to those of exercise training. Med Hypotheses 2009;73:103-105.
[34] Beever R. The effects of repeated thermal therapy on quality of life in patients with type II diabetes mellitus. J Altern Complement Med 2010;16:677-681.
[35] Bathaie SZ, Jafarnejad A, Hosseinkhani S, Nakhjavani M. The effect of hot-tub therapy on serum Hsp70 level and its benefit on diabetic rats: a preliminary report. Int J Hyperth 2010;26:577-585.
[36] Hooper PL, Balogh G, Rivas E, Kavanagh K, Vigh L. The importance of the cellular stress response in the pathogenesis and treatment of type 2 diabetes. Cell Stress Chaperon. 2014;19:447-464.
[37] Hayden MR, Sowers KM, Pulakat L, Joginpally T, Krueger B, Whaley-Connell A. Possible mechanisms of local tissue renin-angiotensin system activation in the cardiorenal metabolic syndrome and type 2 diabetes mellitus. Cardiorenal Med 2011;1:193-210.
[38] Karpe PA, Tikoo K. Heat Shock Prevents Insulin Resistance–Induced Vascular Complications by Augmenting Angiotensin-(1-7) Signaling. Diabetes 2014;63:1124-1139.
[39] Rosas PC, Nagaraja GM, Kaur P, Panossian A, Wickman G, Garcia LR. Hsp72 (HSPA1A) prevents human islet amyloid polypeptide aggregation and toxicity: a new approach for type 2 diabetes treatment. PloS one 2016;11:e0149409
[40] Walter J, Crinnion ND. Sauna as a valuable clinical tool for cardiovascular, autoimmune, toxicant-induced and other chronic health problems. Altern Med Rev 2011;16:215:225.
[41] Zargaran A, Zarshenas MM, Mehdizadeh A, Mohagheghzadeh A. Oxymel in medieval Persia. Pharm Hist (Lond). 2012;42:11-13.
[42] Derakhshandeh-Rishehri, SM. Effect of honey vinegar syrup on blood sugar and lipid profile in healthy subjects. IJPM 2014;5:1608.
[43] Ibn Nafis. Al-mojez fi-teb. Dar-ol-mahajat-ol-baizaa. Beirut 1986; p 22. [in Arabic]
[44] Montagna W. Cutaneous comparative biology. Arch Dermatol 1971;104:pp 577-579.
[45] Skovsø S. Modeling type 2 diabetes in rats using high fat diet and streptozotocin, J Diabetes Invest 2014;5:349-358.