3-1-2013

Effect of Passive Vibration on Skin Blood Flow in Good Glycemic Control and Poor Glycemic Control Type 2 Diabetics

Kanikkai Steni Balan Sackiriyas
Loma Linda University

LOMA LINDA UNIVERSITY
School of Allied Health Professions
in conjunction with the
Faculty of Graduate Studies

Effect of Passive Vibration on Skin Blood Flow in Good Glycemic Control and Poor Glycemic Control Type 2 Diabetics

by

Kanikkai Steni Balan Sackiriyas

A Dissertation submitted in partial satisfaction of
the requirements for the degree
Doctor of Science in Physical Therapy

March 2013

Each person whose signature appears below certifies that this dissertation in his/her opinion is adequate, in scope and quality, as a dissertation for the degree Doctor of Science.

_____, Chairperson

Everett B. Lohman III, Professor of Physical Therapy, Assistant Dean for Graduate Academic Affairs

_____

Lee S. Berk, Associate Professor of Physical Therapy, Director of Clinical Molecular Research Laboratory

_____

Rafael Canizales, Assistant Professor, Associate Dean of the Faculty of Graduate Studies

_____

Noha S. Daher, Associate Professor of Epidemiology and Biostatistics

_____

Ernie Schwab, Associate Professor, Associate Dean for Academic Affairs

ACKNOWLEDGEMENTS

“A kindness done in the hour of need may itself be small, but in worth it exceeds the whole world”
- verse 102, Thirukkural.

It is with immense gratitude that I acknowledge everyone who has contributed to make this dissertation a success. This journey wouldn’t have been the same if not for God, the committee members, my family and friends.

First and foremost, I thank God for keeping my faith alive and helping me tread forward. I would have never been able to complete my dissertation successfully without his grace and compassion.

I wish to extend my deepest gratitude to my advisor/committee chair Dr. Everett B. Lohman who has been a constant source of inspiration. I will always remember the continuous effort he invested in making me a leader by providing a challenging and an admirable environment while conducting my research. It would not have been possible without his invaluable time, brain-storming sessions, belief and guidance as a mentor during my education at Loma Linda. I truly thank Dr.Lohman and his family for nurturing and embracing me forever. As a whole, I would like to thank him for allowing me to grow independently and for playing an instrumental role in various phases of my research and personal life.

I would sincerely extend my thanks to Dr. Noha S. Daher for her priceless time in the data analysis and her unyielding motivation throughout. Her exceptional guidance in writing and everlasting encouragement through her friendship positively changed my perspective about life.

I would like to express my gratitude to Dr. Rafael Canizales for his interest and valid suggestions that contributed in maintaining the accuracy of the format and design of my dissertation. His invaluable help allowed me to introduce my research defense through powerful Prezi presentation software to my friends and colleagues.

I am very grateful to Dr. Lee Berk for his precious guidance and suggestions. His in-depth knowledge in the areas of Whole: Mind. Body truly inspired me and accelerated my interest in the field of medicine and research.

I would like to thank Dr. Ernie Schwab for his meticulous advises from the beginning to the end of my dissertation. I admire his classicality in the field of science and his simplicity in respecting the new scholars. I am very thankful for his positive feedback and showing a special interest to entwine me in the family of the Department of Physical Therapy, Loma Linda University.

A special thanks to Sondra Caposio for her patience, compassionate care and for providing an enjoyable and a memorable working environment.

The support that I received from my research team was immense and greatly helped me to see the in-depth details in my research topic. A special thanks to the research team members: Dr. Gurinder S. Bains, Kinjal S. Solani, Chandip K. Raju, Kulbhushan H. Dhamane, Brijesh K. Singh, Gabriel Paceheco, Samia Alqabbani, Drasti Shah, Charmi Desai, and Fumi Ishhiki.

As always, my wife Savitha and her enduring love, sacrifice, dedication and moral strength remains instrumental in guiding me to tread in the right direction. This work is a shared dream of hers. A very special thanks to my life's wonder, my daughter

Sandhya Immaculate Mercy. Her innocent love and magical smile keeps my heart beating and enlightens my life. I am ever grateful to their persistent support.

I would like to sincerely thank my mother Mats Mary Sackiriyas and my father Sackiriyas Arockiya Swamy for their faith in me and for always being my guiding light. Also, I am indebted and express my thanks to my sithi Vasanthi Joseph and sithappa Joseph for their love and financial support. Honestly, this work would have not been possible without the love and support from my parents, my sister Jenifer Joseph and my brothers Alex Sackiriyas, Paul Jose Sackiriyas, and Jose Joseph.

I wish to wholeheartedly thank my friend Paul Uyeda and his parents Masaji Uyeda and Nobuko Uyeda for their endearment as well as promoting my spiritual outlook. I will always cherish them for their love and accepting me as family.

I would like to express my thanks to my friends Ravi Velusamy, Yazhmozhi Ravi, Ramya Chithra, Gopinath Thippareddy, Balachandran Damodharan, Yashvanth Kuderu, Tirupathi Chindam, Vengatesh Murugesan, Chethan Gowde and Praveen Rajaram for being the pillars in all the possible ways in this long journey. This was possible because of their continuous cheering and motivation, for which I am grateful.

Last but not least I thank my subjects for their precious time and co-operation.

CONTENTS

FIGURES

Figures Page

TABLES

ABBREVIATIONS

DFU	Diabetic Foot Ulcer
T2D	Type 2 Diabetics
SBF	Skin Blood Flow
ST	Skin Temperature
BP	Blood Pressure
GG	Good Glycemic
PG	Poor Glycemic
PV	Passive Vibration
DM	Diabetes Mellitus
CDC	The Centers for Disease Control and Prevention
LADA	Latent Autoimmune Diabetes in Adults
NO	Nitric Oxide
ml	Milliliter
min	Minute
TPR	Total Peripheral Resistance
ADH	Antidiuretic Hormone
AVA	Arteriovenous Anastomoses
NUTR	Nutritive

ABSTRACT OF THE DISSERTATION

Effect of Passive Vibration in Skin Blood Flow, Skin Temperature and Blood Pressure In Good Glycemic Control and Poor Glycemic Control Type 2 Diabetics

by

Kanikkai Steni Balan Sackiriyas

Doctor of Science, Graduate Program in Physical Therapy
Loma Linda University, March 2013
Dr. Everett B. Lohman, Chairperson

Microcirculation regulated by the sympathetic system and vascular endothelium plays a significant role in the homeostasis of temperature and wound healing. Damage to the autonomic nervous system and endothelial system resulting from aging and diabetes decreases the potential of wound healing. Insulin resistance and impaired wound healing associated with type 2 diabetes can lead to diabetic foot ulceration (DFU). Factors such as the increased insulin resistance, impaired wound healing and DFU can increase the risk of amputation in type 2 diabetics (T2D). In research, passive vibration (PV) was effective in increasing skin blood flow (SBF) in healthy individuals as well as in good to fair glycemic control T2D. There has been no study performed to examine the effect of PV on (SBF), skin temperature (ST) and blood pressure (BP) in good glycemic control (GG) control and poor glycemic (PG) control T2D. The purpose of this study was to examine the effect of PV on SBF without adversely affecting the ST and BP in GG control and PG control T2D. This was done by assessing SBF using a MOOR full-field laser perfusion imager (MOOR FLPI) after the application of PV.

Seventeen good glycemic control and fifteen poor glycemic control T2D participated in this study. The SBF, ST and BP were measured at the baseline. Then, the

subjects received PV to their calf area and foot area on another side for about ten minutes. The second reading was measured immediately after the PV. The third measurement was taken after a ten minutes rest post the vibration application.

Results from this study showed that PV significantly increased SBF in the calf area from baseline to immediately after vibration and baseline to 10 minutes post rest without adversely affecting the ST and BP in both GG control and PG control T2D. Also, the percent change of SBF in the foot area was higher in the GG control (91.3%) than in PG control T2D (32.6%).

Results from this study suggest that PV can be a safe and alternative method in increasing SBF without increasing the risk of burns in GG control and PG control T2D.

CHAPTER ONE

INTRODUCTION

Diabetes Mellitus (DM) is a common metabolic disorder in which the pancreatic cells produce either no insulin or insufficient insulin, or the body cells do not respond to the insulin that is produced. It results in abnormal metabolism of carbohydrates, fats and proteins which leads to a high amount of glucose levels in the blood stream and in the urine [(1)]. Diabetes has become a major health care problem in the United States [(2)], affecting millions of Americans each year [(3)]. It is estimated that 25.8 million (8.3%) children and adults in the United States have diabetes and 10.9 million (26.9%) of the world population ≥65years have diabetes [(1), (2)]. The Centers for Disease Control and Prevention (CDC) estimated that diagnosed diabetes is likely to increase 165 percent by 2050 [(1)].

Diabetes is one of the leading causes of disability and death from stroke and heart diseases. It is the seventh leading cause of death in the United States, according to a report published by the CDC [(1), (2)]. The fact sheet released by the National Diabetes Information Clearinghouse reported that the care associated with diabetes has cost the United States a total of $174 billion (indirect costs and direct costs) [(1), (2)]. The medical expenses associated with diabetes are two times higher in diabetic individuals than in non-diabetics [(2)]. Diabetes Mellitus is divided into four major types: Type 1, Type 2, Gestational, and Latent Autoimmune Diabetes in Adults (LADA) [(1), (2), (3), (4)].

Type 1 diabetes is an autoimmune disease in which the body's system for fighting infection (the immune system) turns against the host cells. It attacks and destroys the insulin producing beta cells in the pancreas, resulting in the production of little or no insulin. Causes that are possibly associated with Type I diabetes include a T cell mediated autoimmune attack, hereditary influence, environmental factors, and viruses. Type 1 diabetes is most often present in children and the young adults [(1), (4), (5)].

Patients are categorized as prediabetes when their blood glucose level is higher than the normal but lower than the level used for diagnosing diabetes. Thirty three percent (1 in 3 Americans) of people having prediabetes are likely to develop type 2 diabetes within ten years if adequate steps are not taken [(1), (2)]. In contrast, type 2 diabetes is a non-autoimmune disease [(6)]. Type 2 diabetes is the most common form (90% to 95%) among all types of diabetes and is due to insulin resistance in which target cells do not use the insulin effectively, even though normal, or in some cases elevated levels of circulating endogenous insulin are present in the body. Eventually, insulin production decreases after several years, leading to increased build up of glucose levels in the body [(1)].

Gestational diabetes usually occurs late in the pregnancy due to associated hormonal production or insulin shortage. Women with gestational diabetes have 40% to 60% chance of developing into type 2 diabetes within 5 to 10 years [(1)].

Latent autoimmune diabetes in adults (LADA) is also called type 1.5 diabetes or double diabetes, because it shows combined signs of both type 1 and type 2 diabetes [(1)]. The LADA is an autoimmune disease and shows the clinical symptoms of type 1 diabetes. According to the Immunology of Diabetes Society, there are three diagnostic

criteria for the LADA: 1) Adult age of onset (30 years of age); 2) presence of at least one autoantibody (GAD, ICA, IAA or IA-2), and 3) insulin dependence for the first six months after the diagnosis [7], [8].

Regardless of the type of diabetes mellitus (DM), there are numerous complications associated with diabetes, including heart disease, stroke, high blood pressure, blindness, kidney disease, neuropathy, poor circulation, foot ulcers and amputation [2]. The most common complication associated with diabetes is damage to the microcirculation and endothelial cells [9]. Damage to endothelial cells reduces their ability to produce nitric oxide (NO) and decreases their sensitivity to NO, thereby leading to decreased skin blood flow [10], [11]. Microangiopathy due to defects in the structure and function of the vessel wall, and impaired hemodynamic (hyper dynamic) circulation is a common feature in diabetes. Anatomical impairments of the vessel wall can include glycocalyx on the luminal side and protein deposition, smooth muscle cell proliferation on the abluminal side. Impaired hemodynamics resulting from increased plasma volume and viscosity, reduction in erythrocyte deformability, and aggregation of blood cells can lead to microangiopathy, a common characteristic in diabetes [12], [13]. Endothelial glycocalyx reduces the internal diameter of the capillaries and reduces availability of oxygen delivery to the tissues by as much as 60% [13], [14]. Capillary rarefaction due to hypertension in diabetes increases diffusion distance between capillaries and target cells, slowing down diffusion rates of oxygen and glucose between those structures [13].

Blood Circulation

The entire blood circulation in the body is about 5-6 L/m at rest. A total of 4.75 L/m is distributed to the following organs; liver and kidneys 2,500 ml/min, skeletal muscles 1,000 ml/min, brain 750 ml/min, heart 250 ml/min, and skin 250 ml/min (thermo-neutral environments). The remaining cardiac output is delivered to other organs [(15), (16)]. Blood flow is regulated by factors such as arterial pressure, vascular resistance, total peripheral resistance (TPR), blood viscosity, and length and radius of the blood vessel. Blood flow increases proportionately with increasing arterial pressure and decreases with vascular resistance. The principal factor in regulation of blood flow is the radius of the vessel since all other factors do not change significantly in a healthy individual. For example, a decrease in the diameter of the blood vessel to half of its size increases resistance and reduces blood flow by 16 times when all other factors are constant [(15)].

The vascular system is divided into larger conduit, medium resistance and smaller micro vessels. Resistance vessels are responsible for maintaining blood pressure. Micro vessels are entirely different from macro and medium vessels and represent "nutritive" structures [(13), (17)].

Regulation of Blood Pressure

Blood flow is regulated by two classes of mechanisms; those that are extrinsic, and those that are intrinsic to the system proper. Extrinsic mechanisms act through the autonomic nervous system and endocrine system, and produce more generalized effects in many regions of the body. They directly affect resistance and blood flow. Intrinsic

mechanisms within individual tissues have "built in" (localized) effects on vascular resistance and blood flow. Intrinsic mechanisms regulate blood circulation through myogenic and metabolic control [15].

Extrinsic Control

The autonomic nervous system controls blood flow through sympathetic (alpha-adrenergic, beta-adrenergic) and parasympathetic (cholinergic) innervation. Endocrine system controls blood flow through hormones such as Angiotensin II, Vasopressin (ADH), Histamine, Bradykinens, and Prostaglandins [15].

Intrinsic Control

Intrinsic mechanisms control circulation through auto regulation. Autoregulation through myogenic and metabolic regulation allows the organ to have some independent control to maintain a constant blood flow rate despite variations in the systemic blood pressure [15].

Skin Circulation

Skin circulation is a highly regulated mechanism that plays a vital role in the regulation of blood pressure, temperature and healing, and is controlled by the central nervous system and local metabolic states of tissues [16], [18], [19]. Micro vessels consist of a single terminal feeding arteriole that branch into a group of 15-20 smaller diameter capillaries [13], [17]. Microcirculation carries fuel and nutrients to remote cells and involves in the exchange of waste products with the surrounding tissues. It is influenced by

vascular permeability which in turn depends on the structure of vessel walls and existing hydrostatic pressure differences between arteriolar and venular segments [13]. The metabolic, physical and nervous systems regulate the microcirculation. Therefore, not the quantity but the distribution of blood in the micro vascular bed is a primary determinant. A continuous change of blood flow in relation to amount, velocity and direction due to local metabolic needs is finely regulated by vasoconstriction and vasodilation in the microcirculation. This is achieved through the arteriolar myogenic response, venoarteriolar reflex, and precapillary arteriolar vasomotion [13], [20]. Failure in these mechanisms can lead to hyperperfusion and subsequent hypertension in the micro vascular bed.

The architecture of the micro vascular system is not uniform and varies in glabrous (non hairy) and nonglabrous (hairy) skin [21]. The glabrous skin (palms, soles, lips, face, tips of fingers and toes) has numerous thick walled thermo-regulating arteriovenous anastomoses (AVA) [22]. It is mainly innervated by sympathetic vasoconstrictor nerves [16], [21], [23], [24]. Numerous larger diameter arterioles and venules in these areas allow low resistance, high blood flow directly from the arterioles to venules [16], [21], [25], [26], [27], [28]. In contrast to that, the nonglabrous skin (dorsal area of hand, foot) has more nutritive (NUTR) perfusion through small capillaries with fewer AVA and is controlled by both the sympathetic vasoconstrictor and vasodilator nerves [24], [29]. These differences may lead to differential skin blood flow rates.

Capillaries in the microcirculation have only one single endothelial cell layer on their basement membrane [13]. Vascular endothelial cells are placed in between the blood and surrounding vascular smooth muscles [30], [31]. They secrete fat soluble chemicals such

as vasodilators and vascular relaxation factors [27], [32]. These chemicals diffuse into the blood and the vascular smooth muscles, and the balance between these factors maintains the normal skin blood flow. Any increase or decrease in these factors in one direction can change the luminal size of the arterioles and thereby leading to increased or decreased blood flow [27], [32], [33], [34], [35], [36].

Skin blood flow can be influenced by various factors such as tissue local pressure and occlusion, temperature, moist heat, aging and diabetes, vitamins, body mass index and race. Measuring SBF helps to understand the function of various organs and their reaction to various stimuli and pharmacological interventions [37]. Skin blood flow can be measured by direct capillary pressure measurement, transcutaneous oxygen measurement, radionuclide techniques, temperature (biopac thermostat, radiometric, thermography, microwave radiometry and thermal clearance or conductivity measurements), ultrasound, dermofluorometry, laser doppler flowmetry, photoplethysmography, and capillary microscopy [38].

Vibration

Mechanical oscillations applied randomly or periodically are known as vibration. Vibration can be applied to the whole body or to a specific region of the body. Vibration can be divided into active and passive vibration. In active vibration, the mechanical vibration is delivered horizontally to the body part and requires that the patient actively participate in weight bearing and exercise [39].

Passive vibration does not require the patient to bear weight and the mechanical oscillations are delivered perpendicularly with the subjects relaxed [39]. Studies conducted

on vibration reported changes associated with the vibration such as increased muscular strength [40], [41], [42], [43], [44], improved muscle performance and balance [45], [46], [47], increased muscle flexibility [48], increased body composition [42], [49], improvements in human athletic performance such as running parameters and jumping, and improved circulation [40], [47], [50], [51].

References

1. National Diabetes Information Clearinghouse. (April 2012). Diabetes Overview. Retrieved April 30, 2012. from http://diabetes.niddk.nih.gov/dm/pubs/overview/index.aspx [database on the Internet]. Available from: http://diabetes.niddk.nih.gov/dm/pubs/overview/index.aspx.

2. Centers for Disease Control and Prevention. National diabetes fact sheet: national estimates and general information on diabetes and prediabetes in the United States, 2011. Atlanta, GA: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, 2011.

3. Ziegler D. Diabetic cardiovascular autonomic neuropathy: prognosis, diagnosis and treatment. Diabetes Metab Rev. 1994 Dec;10(4):339-83.

4. Sumpio BE. Foot ulcers. New Engl J Med. 2000 Sep 14;343(11):787-93.

5. Rother KI. Diabetes treatment--bridging the divide. N Engl J Med. 2007 Apr 12;356(15):1499-501.

6. Palmer JP, Hampe CS, Chiu H, Goel A, Brooks-Worrell BM. Is latent autoimmune diabetes in adults distinct from type 1 diabetes or just type 1 diabetes at an older age? Diabetes. 2005 Dec;54:S62-S7.

7. Guglielmi C, Palermo A, Pozzilli P. Latent autoimmune diabetes in the adults (LADA) in Asia: from pathogenesis and epidemiology to therapy. Diabetes Metab Res Rev. 2012 Dec;28 Suppl 2:40-6.

8. Gale EA. Latent autoimmune diabetes in adults: a guide for the perplexed. Diabetologia. 2005 Nov;48(11):2195-9.

9. Rendell M, Bamisedun O. Skin Blood-Flow and Current Perception in Pentoxifylline-Treated Diabetic Neuropathy. Angiology. 1992 Oct;43(10):843-51.

10. Hogikyan RV, Galecki AT, Pitt B, Halter JB, Greene DA, Supiano MA. Specific impairment of endothelium-dependent vasodilation in subjects with type 2 diabetes independent of obesity. J Clin Endocrinol Metab. 1998 Jun;83(6):1946-52.

11. Caballero AE, Arora S, Saouaf R, Lim SC, Smakowski P, Park JY, et al. Microvascular and macrovascular reactivity is reduced in subjects at risk for type 2 diabetes. Diabetes. 1999 Sep;48(9):1856-62.

12. Le Devehat C, Khodabandehlou T, Vimeux M. Impaired hemorheological properties in diabetic patients with lower limb arterial ischaemia. Clin Hemorheol Microcirc. 2001;25(2):43-8.

13. Wiernsperger NF, Bouskela E. Microcirculation in insulin resistance and diabetes: more than just a complication. Diabetes Metab. 2003 Sep;29(4 Pt 2):6S77-87.

14. Kindig CA, Sexton WL, Fedde MR, Poole DC. Skeletal muscle microcirculatory structure and hemodynamics in diabetes. Respir Physiol. 1998 Feb;111(2):163-75.

15. Fox SI. Human Physiology. Dubuque, Iowa: Wm. C. Brown; 1984. p. 314-45.

16. Charkoudian N. Skin blood flow in adult human thermoregulation: how it works, when it does not, and why. Mayo Clin Proc. 2003 May;78(5):603-12.

17. Berg BR, Cohen KD, Sarelius IH. Direct coupling between blood flow and metabolism at the capillary level in striated muscle. Am J Physiol. 1997 Jun;272(6 Pt 2):H2693-700.

18. Petrofsky J, Lee S. The effects of type 2 diabetes and aging on vascular endothelial and autonomic function. Med Sci Monit. 2005 Jun;11(6):CR247-54.

19. Berne RM, Levy MN. Principles of Physiology. 4 ed. St. Louis, MO: Mosby; 2005.

20. Wiernsperger NF. In defense of microvascular constriction in diabetes. Clin Hemorheol Microcirc. 2001;25(2):55-62.

21. Rendell MS, Milliken BK, Finnegan MF, Finney DA, Healy JC. The skin blood flow response in wound healing. Microvasc Res. 1997 May;53(3):222-34.

22. Bornmyr S, Svensson H, Lilja B, Sundkvist G. Skin temperature changes and changes in skin blood flow monitored with laser Doppler flowmetry and imaging: a methodological study in normal humans. Clin Physiol. 1997 Jan;17(1):71-81.

23. Lossius K, Eriksen M, Walloe L. Fluctuations in blood flow to acral skin in humans: connection with heart rate and blood pressure variability. J Physiol. 1993 Jan;460:641-55.

24. Johnson JM, Proppe DW. Cardiovascular adjustments to heat stress. In: Fregly MJ, Blatteis CM, editors. Handbook of Physiology: Oxford University Press; 1996. p. 215-43.

25. Hales JR, Jessen C, Fawcett AA, King RB. Skin AVA and capillary dilatation and constriction induced by local skin heating. Pflugers Arch. 1985 Jul;404(3):203-7.

26. Popoff N. The digital vascular system. Arch Pathol. 1934;18:295-330.

27. Rowell LB. Reflex control of the cutaneous vasculature. J Invest Dermatol. 1977 Jul;69(1):154-66.

28. Zweifach BW, Lipowsky HH. Pressure-flow relations in blood and lymph microcirculation. In: Renkin EM, Michel CC, Geiger SR, editors. Handbook of Physiology The Cardiovascualr System. Oxford: Oxford Univ; 1987. p. 251-308.

29. Johnson JM, Brengelmann GL, Hales JR, Vanhoutte PM, Wenger CB. Regulation of the cutaneous circulation. Fed Proc. 1986 Dec;45(13):2841-50.

30. Farage MA, Miller KW, Elsner P, Maibach HI. Functional and physiological characteristics of the aging skin. Aging Clin Exp Res. 2008 Jun;20(3):195-200.

31. Triggle CR, Ding H. The endothelium in compliance and resistance vessels. Front Biosci (Schol Ed). 2011;3:730-44.

32. Fox RH, Edholm OG. Nervous control of the cutaneous circulation. Br Med Bull. 1963 May;19:110-4.

33. Charkoudian N, Johnson JM. Reflex control of cutaneous vasoconstrictor system is reset by exogenous female reproductive hormones. J Appl Physiol. 1999 Jul;87(1):381-5.

34. Petrofsky J, Goraksh N, Alshammari F, Mohanan M, Soni J, Trivedi M, et al. The ability of the skin to absorb heat; the effect of repeated exposure and age. Med Sci Monit. 2011 Jan;17(1):CR1-8.

35. Behrendt D, Ganz P. Endothelial function. From vascular biology to clinical applications. Am J Cardiol. 2002 Nov 21;90(10C):40L-8L.

36. Ding H, Triggle CR. Endothelial cell dysfunction and the vascular complications associated with type 2 diabetes: assessing the health of the endothelium. Vasc Health Risk Manag. 2005;1(1):55-71.

37. Petrofsky JS. Resting Blood Flow in the Skin: Does it Exist, and What Is the Influence of Temperature, Aging, and Diabetes. J Diabetes Sci Technol. [Review Article]. 2012;6(3):1-11.

38. Swain ID, Grant LJ. Methods of measuring skin blood flow. Phys Med Biol. 1989 Feb;34(2):151-75.

39. Lohman EB, Bains G, Lohman T, Deleon M, Perrofsky JS. A comparison of the effect of a variety of thermal and vibratory modalities on skin temperature and blood flow in healthy volunteers. Med Sci Monit. 2011;17(9):MT72-MT81.

40. Delecluse C, Roelants M, Diels R, Koninckx E, Verschueren S. Effects of whole body vibration training on muscle strength and sprint performance in sprint-trained athletes. Int J Sports Med. 2005 Oct;26(8):662-8.

41. Delecluse C, Roelants M, Verschueren S. Strength increase after whole-body vibration compared with resistance training. Med Sci Sports Exerc. 2003 Jun;35(6):1033-41.

42. Roelants M, Delecluse C, Verschueren SM. Whole-body-vibration training increases knee-extension strength and speed of movement in older women. J Am Geriatr Soc. 2004 Jun;52(6):901-8.

43. Roelants M, Delecluse C, Goris M, Verschueren S. Effects of 24 weeks of whole body vibration training on body composition and muscle strength in untrained females. Int J Sports Med. 2004 Jan;25(1):1-5.

44. Roelants M, Verschueren SM, Delecluse C, Levin O, Stijnen V. Whole-body-vibration-induced increase in leg muscle activity during different squat exercises. J Strength Cond Res. 2006 Feb;20(1):124-9.

45. Runge M, Rehfeld G, Resnicek E. Balance training and exercise in geriatric patients. J Musculoskelet Neuronal Interact. 2000 Sep;1(1):61-5.

46. Torvinen S, Kannu P, Sievanen H, Jarvinen TA, Pasanen M, Kontulainen S, et al. Effect of a vibration exposure on muscular performance and body balance. Randomized cross-over study. Clin Physiol Funct Imaging. 2002 Mar;22(2):145-52.

47. Torvinen S, Kannus P, Sievanen H, Jarvinen TA, Pasanen M, Kontulainen S, et al. Effect of four-month vertical whole body vibration on performance and balance. Med Sci Sports Exerc. 2002 Sep;34(9):1523-8.

48. Di Giminiani R, Manno R, Scrimaglio R, Sementilli G, Tihanyi J. Effects of individualized whole-body vibration on muscle flexibility and mechanical power. J Sports Med Phys Fitness. 2010 Jun;50(2):139-51.

49. Vissers D, Verrijken A, Mertens I, Van Gils C, Van de Sompel A, Truijen S, et al. Effect of long-term whole body vibration training on visceral adipose tissue: a preliminary report. Obes Facts. 2010;3(2):93-100.

50. Paradisis G, Zacharogiannis E. Effects of whole-body vibration training on sprint running kinematics and explosive strength performance. J Sport Sci Med. 2007 Mar;6(1):44-9.

51. Rittweger J, Beller G, Felsenberg D. Acute physiological effects of exhaustive whole-body vibration exercise in man. Clin Physiol. 2000 Mar;20(2):134-42.

CHAPTER TWO

EFFECT OF PASSIVE VIBRATION ON SKIN BLOOD FLOW IN GOOD GLYCEMIC CONTROL AND POOR GLYCEMIC CONTROL TYPE 2 DIABETICS

Kanikkai Steni Balan Sackiriyas, MPT

Everett B. Lohman, DSc

Noha S. Daher, DrPH

Lee S. Berk, DrPH

Rafael Canizales, PhD

Ernie Schwab, PhD

Dept. of Physical Therapy, School of Allied Health Professions
Loma Linda University, Loma Linda, California, USA

Abstract

Objective

To study the effect of passive vibration on skin blood flow (SBF) in two groups of diabetics: good control and poor control.

Materials and Methods

Passive vibration using Power Plate® was applied to the calf area and the plantar surface of the foot. Fifteen good glycemic control (HbA1c < 7.5%) and twelve poor glycemic control (HbA1c > 9%) type 2 diabetics participated in this study. The SBF was measured using a MOOR full-field Laser perfusion imager before, immediately after vibration and 10 minutes post the vibration application.

Results

There was a significant difference in the mean SBF for the calf area from baseline to immediately after vibration in both good glycemic control and poor glycemic control diabetics. The mean calf SBF was almost doubled in good glycemic control diabetics from baseline (38.9 flux) to immediately after vibration (69.5 flux) ($p=.03$). The mean calf SBF was more than doubled in poor glycemic control diabetics from baseline (32.9 flux) to immediately after vibration (77.9 flux) ($p=.02$). However, no significant change in mean SBF was detected over time for the foot area in good glycemic control and poor glycemic control diabetics ($p<.05$). Baseline resting SBF was higher in foot than calf area for both good glycemic control and poor glycemic control type 2 diabetics. The percent change from baseline to immediately after vibration in the calf SBF was higher in poor

glycemic control (132.6%) than the good glycemic control diabetics (76%). Foot SBF showed a higher percent increase in the good glycemic control (72.3%) than the poor glycemic control diabetics (32.1%). The percent increase was 100.3% in the calf SBF and 55% in foot SBF irrespective of group.

Conclusion

In this study, we observed a significant change in mean calf SBF from baseline to immediately after vibration. Also, the higher percent change of calf SBF and foot SBF was observed from baseline to immediately after vibration. These results suggest that passive vibration may be an effective therapy for increasing lower extremity circulation in both good glycemic control and poor glycemic control type 2 diabetics.

Key Words

Vibration, MOOR FLPI, Skin Circulation, Good Glycemic Control, Poor Glycemic Control, Diabetes Mellitus, Full-field Laser Perfusion Imager.

ABBREVIATIONS

DM	Diabetes Mellitus
T2D	Type 2 Diabetics
CDC	The Centers for Disease Control and Prevention
HbA1c	Hemoglobin Assay A1c
BMI	Body Mass Index
AVA	Arteriovenous Anastomoses
SBF	Skin Blood Flow
NUTR	Nutritive
PV	Passive Vibration
NO	Nitric Oxide
ml	Milliliter
min	Minute
DVT	Deep Vein Thrombosis
LLU	Loma Linda University
FLPI	Full-field Laser Perfusion Imager
SPSS	Statistical Product and Service Solutions
SD	Standard Deviation
SE	Standard Error
DFU	Diabetic Foot Ulcer
PVD	Peripheral Vascular Diseases

Introduction

Diabetes Mellitus (DM) is a major health care problem and can lead to stroke and heart disease [(1)]. Millions of Americans are affected by DM. The associated medical expenses and death rate is two times higher in diabetics than non-diabetics [(1), (2)]. The highest incidence of diabetes is known as type 2 diabetes (T2D) (90% to 95 %). This typically results from the inadequate use of insulin by target cells even though circulating insulin level maybe normal or elevated [(1), (2), (3)]. According to the Center for Disease Control and Prevention (CDC), DM is classified into good glycemic (HbA1c <7.5%), fair glycemic (HbA1c ≥7.5% to ≤9%) and poor glycemic control (HbA1c >9%) based on the Hemoglobin A1c (HbA1c) level [(4), (5)].

Circulation

Tissue healing is an intricate process and primarily depends on blood circulation [(6)]. Skin circulation is under the control of central nervous system and tissue's metabolic state [(7)]. Resting skin blood flow is dependent on factors such as skin moisture, tissue pressure, age, vitamins, race, diabetes, and exposure to free radicals [(8)].

Aging, body mass index (BMI) and diabetes affect endothelial cells and autonomic function, hence decreases microcirculation [(6), (9), (10)]. Complex architecture of skin is responsible for differential circulation rate. Glabrous skin (palms, soles) has thick walled arteriovenous anastomoses (AVA). Numerous larger arteries and venules in these areas allow low resistance and high skin blood flow (SBF) rate. Whereas, non-glabrous skin (forearm, calf, dorsal hand) has more nutritive (NUTR) perfusion and is served by capillaries with fewer AVA [(11), (12), (13)].

In research, vibration is being used to increase skin circulation. Research supports the use of passive vibration (PV) to improve skin blood flow (SBF) without increasing the risk of burns. Lohman et al., (2012) showed that PV significantly improved SBF in hairy and non-hairy skin both in good to fair glycemic control diabetics and non-diabetics [14], [15], [16]. The purpose of this study was to examine the effect of PV on SBF in good glycemic control versus poor glycemic control type 2 diabetics. We hypothesized that passive vibration induced increase in SBF in calf and foot were higher in good glycemic control than the poor glycemic control diabetics. The secondary hypothesis was that passive vibration induced increase in SBF was higher in calf (non-glabrous) than the foot (glabrous) in both good glycemic control and poor glycemic control type 2 diabetics.

Material and Methods

Study Population

Type 2 diabetics between the age ranges of 18-75 years invited to participate in this study. Subjects with neurological disorders, orthopedic disorders, bleeding disorders, leg ulcer, chronically exposed to vibration, cardiovascular diseases, deep vein thrombosis (DVT), or pregnant were excluded. Thirty two subjects were recruited from the Diabetes Support Group and from the Diabetes Treatment Center at Loma Linda University (LLU) Medical Center. Five subjects were excluded because they did not meet the inclusion criteria. Subjects were assigned into one of two groups: Good glycemic control diabetics and Poor glycemic control diabetics. Both groups received passive vibration to their calf area and the opposite foot area on the same day. The LLU's institutional review board

approved all procedures and subjects signed statements of informed consent (Appendix A).

Instrumentation

A Physio Plate® (Domino S.R.L, San Vendemiano, Italy) was used to deliver passive vibration at a frequency of 50 Hz for a total number of ten cycles (one cycle= 60s working time: 2 s rest time) for a total of approximately ten minutes (Figure 1). A MOOR full-filed Laser perfusion Imager (FLPI) (MOOR FLPI V 2.1, Oxford, England) was pre-warmed for about 30 minutes to stabilize measurements and was used to measure SBF non-invasively (Figure 2). The FLPI uses a red light laser beam applied perpendicularly to capture SBF and blood flow was measured in "Flux" unit.

Figure 1. Physio Plate® vibration platform.

Figure 2. MOOR Full-field Laser Perfusion Imager **(**FLPI).

Procedure

Screening

The testing room temperature was maintained at 71.6°F-75.2°F (22°-24° C) for about 30 minutes before the subject enters. A 30 minutes rest period in supine position was given to subjects to stabilize their blood flow before intervention. Subjects were screened for exclusion and demographic data was collected (Appendix B). Subjects were screened for possible DVT using the Well's criteria [17]. Subjects with a score of ≥2 (high risk) were excluded.

Cutaneous sensation was checked using a Semmes-Weinstein Monofilament (North Coast Medical, Inc, Morgan Hill, CA, USA) and the response, color of the handle and notations were noted on the sensory foot mapping form (Appendix C). Vibration

sense was checked with a 128 Hz tuning fork and subjects with a score of 2 (absent sensation) were excluded.

Testing

Subjects were asked to lie prone on a plinth. A square shaped 3 cm x 3 cm area was marked on the posterior aspect of the calf (muscle belly) and on the plantar aspect of the first three (1-3) metatarsal heads to capture SBF. Baseline SBF was measured in the calf area using the FLPI (Figure 3). Then, subjects received passive vibration to their calf for ten minutes (Figure 4). The second reading was taken immediately after vibration. Subjects were given a ten minutes rest before the third reading was taken. The same procedures were repeated for foot on the opposite leg (Figure 5 & Figure 6).

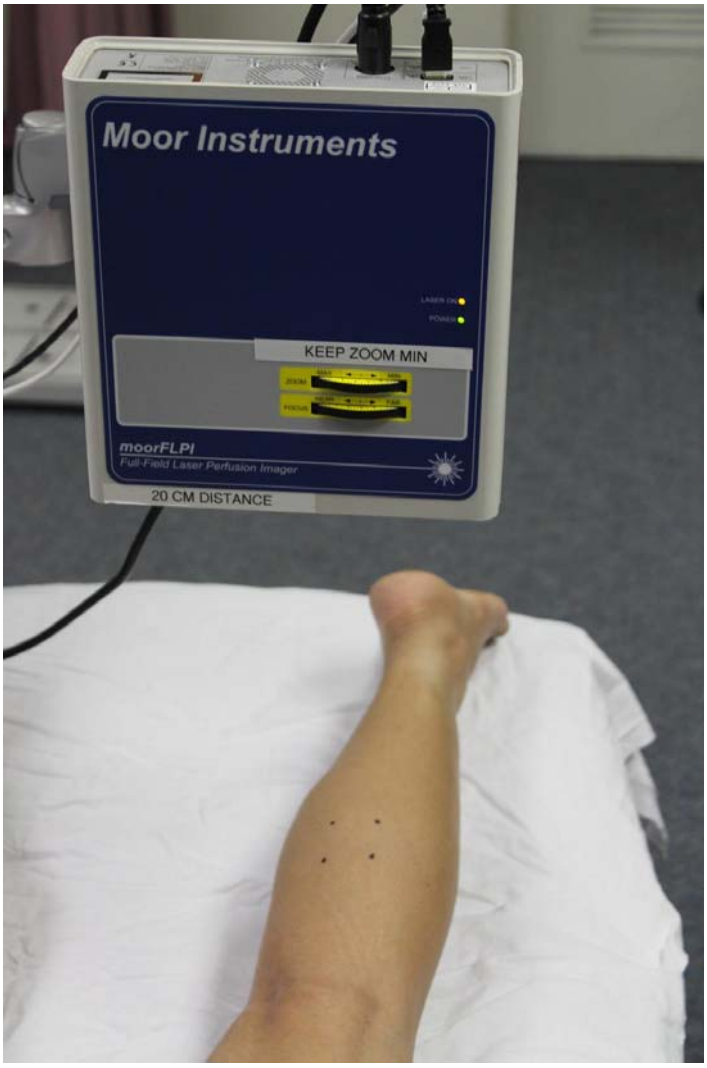


Figure 3. SBF measurement in the calf area.

Figure 4. Calf area vibration.

Figure 5. Foot area vibration.

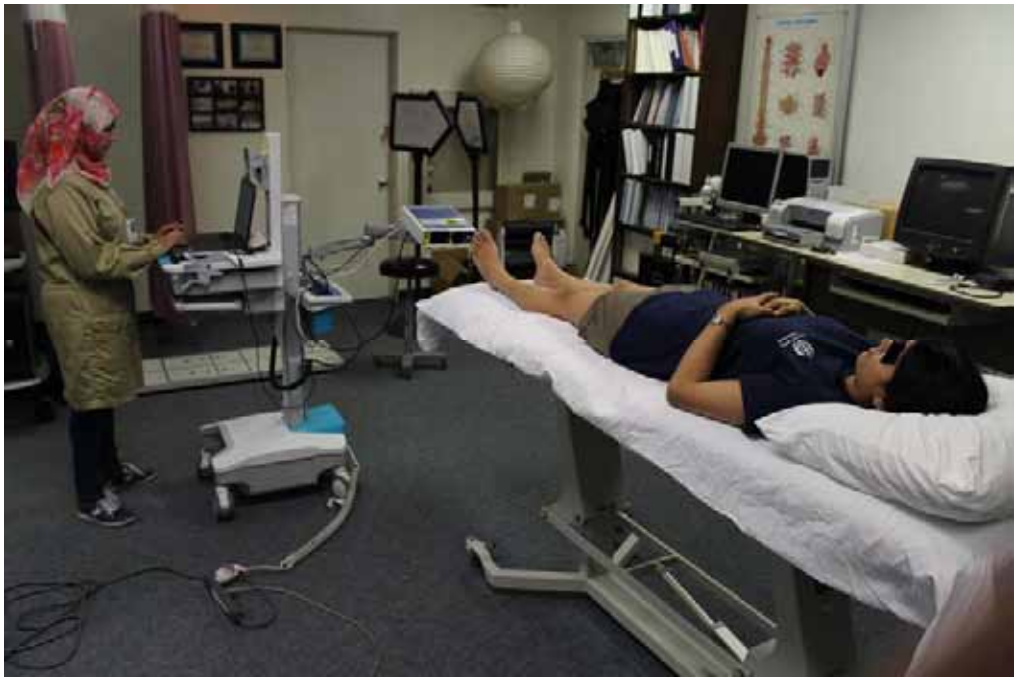


Figure 6. SBF measurement in the foot area.

Data Analysis

Data was analyzed using SPSS version 20.0 [18]. One sample Kolmogorov Smirnov test was used to examine the distribution of the continuous variables. Chi-square test of independence was used to compare the proportions of males & females, ethnicity and levels of physical activity by group. We compared mean age and body mass index (BMI) by group using independent t-test. Mixed factorial analysis of variance was used to compare the effect of passive vibration on SBF from baseline to immediately after vibration and 10 minutes post rest in good glycemic control and poor glycemic control T2D subjects' calf and foot. Significant differences were further examined with Bonferroni test. The level of significance was set at $p<.05$.

Results

Fifteen good glycemic control and twelve poor glycemic control type 2 diabetics participated in the study. The results of the Kolmogorov Smirnov test showed the distribution of age, BMI and SBF were approximately normal. There were no significant differences between the good glycemic and poor glycemic control diabetics in terms of gender, race, physical activity, age and BMI ($p>.05$) (Table 1).

Table 1. Distribution of demographic data by group (N=28).

Variables		Good (n=16)	Poor (n=12)	p-value
Gender†	Male	9 (56.2%)	6 (50%)	.74
	Female	7 (43.8%)	6 (50%)	
Ethnicity†	White	7 (70%)	3 (30%)	.49
	Hispanic	4 (66.79%)	2 (33.3%)	
	Others¶	2 (33.3%)	6 (66.7%)	
	African American	2 (66.7%)	1 (33.3%)	
Physical activity†	Very light	3 (37.5%)	5 (62.5%)	.43
	Light	5 (71.4%)	2 (28.6%)	
	Moderate & Heavy	8 (61.5%)	5 (38.5%)	
Age (Mean±SD)*		62.3±11.4	56.9±7.7	.17
BMI (Mean±SD)*		31.1±5.6	32.0±6.8	.71

†: Chi-square test

*: Independent t test

¶: Others: Asians, Middle eastern

Good Glycemic Control

There was a significant change in mean calf SBF over time in good glycemic control diabetics ($F_{2, 30}$=6.71, p=.02) (Table 2). A significant change was seen between baseline and immediately after vibration (p=.03) and between baseline and 10 minutes post rest (p=.03). However, there was no significant change in mean foot SBF over time in good glycemic control diabetics ($F_{2, 30}$=2.6, p=.11). The mean SBF in the good glycemic control was significantly higher in foot than in calf at baseline (137.5±22.4 vs 38.9±2.3; p<.001), immediately after vibration (187.0±29.2 vs 69.5±12.5; p<.001) and 10 minutes post rest (142.1±21.8 vs 66.8±11.6; p<.01) (Figure 7).

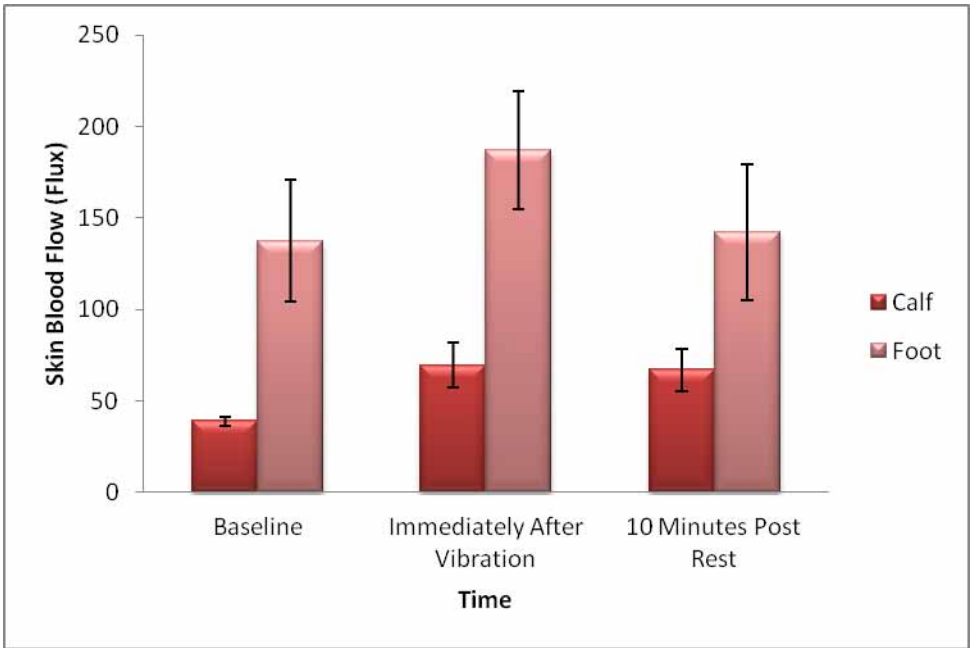


Figure 7. Changes in mean±SE† of SBF† by site in good glycemic control diabetics over time.

†SBF: Skin blood flow

†SE: Standard error

Poor Glycemic Control

There was a significant change in mean calf SBF over time in poor glycemic control diabetics ($F_{2, 22}$=9.8, p=.01) (Table 2). A significant change was detected between baseline and immediately after vibration (p=.02), between baseline and 10 minutes post rest (p=.01). There was no significant change in mean foot SBF over time in poor glycemic control diabetics ($F_{2, 30}$=.04, p=.91). The mean SBF in the poor glycemic control was significantly higher in foot than in the calf at baseline (157.6±33.4 vs 32.9±2.6; p<.01), immediately after vibration (163.8±32.3vs 77.9±15.5; p=.03) and 10 minutes post rest (160.1±37.0 vs 70.9±12.5; p=.04) (Figure 8).

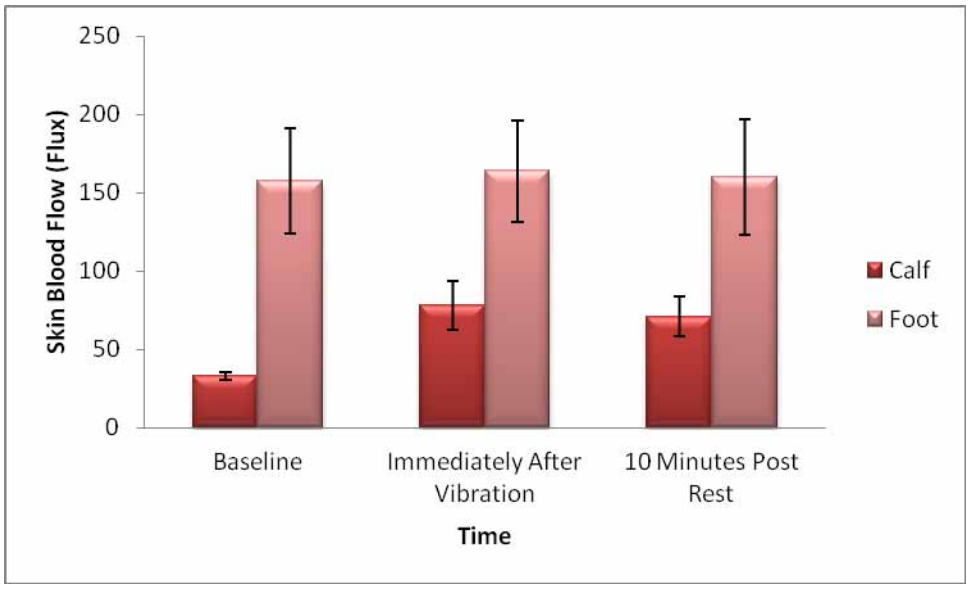


Figure 8. Changes in mean±SE† SBF† by site in poor glycemic control diabetics over time.

†SBF: Skin blood flow
†SE: Standard error

Table 2. Mean (SE†) skin blood flow over time by group and site.

Site	Group	Baseline	Immediately after vibration	10 min post rest	p-value*
Calf	**Good**	38.9(2.3)	69.5(12.5)	66.8(11.6)	.02
	Poor	32.9(2.6)	77.9(15.5)	70.9(12.5)	.01
Foot	**Good**	137.5(22.4)	187.0(29.2)	142.1(21.8)	.11
	Poor	157.6(33.4)	163.8(32.3)	160.1(37.0)	.91

*Analysis of variance
†SE: Standard error

Good Glycemic Control vs. Poor Glycemic Control

There was a significant difference in mean calf SBF over time in both good glycemic control and poor glycemic control diabetics ($F_{2, 52}$=16.6, p=.001). However, there was no significant difference between groups ($F_{2, 30}$=.03, p=.90). Based on the Bonferroni test, there was a significant difference in calf SBF between baseline and immediately after vibration (p=.001) and between baseline and 10 minutes post rest (p=.001) in both good glycemic control and poor glycemic control diabetics. There was no significant difference in mean calf SBF between immediately after vibration and 10 minutes post rest (p=.40). There was no significant difference in foot SBF over time in both good glycemic control and poor glycemic control diabetics ($F_{2, 52}$=1.57, p=.22).

Discussion

The diabetic foot ulcer (DFU) is the leading cause of amputation in diabetics and approximately 8% of diabetics tend to have peripheral vascular disease (PVD) at the time

of initial diagnosis [19]. Peripheral vascular disease rapidly rises with age and duration of diabetes. The associated lower extremity amputation rate is 15 times higher in diabetics than non diabetics. In most cases, the lesion starts from a painless trauma in an insensate neuropathic foot. Healing of these lesions is thwarted by the presence of PVD. Lack of sufficient blood flow and decreased delivery of leukocytes impairs the function of some of tissue growth factors and antibiotics that are oxygen dependant, and increases the growth of highly destructive anaerobes in the infected tissues [19]. Therefore, modalities that can increase even a small amount of circulation may play a clinically important role in the healing process. Studies from the department of physical therapy in Loma Linda University and others have shown that vibration can be effective in increasing SBF in diabetics as well as in non-diabetics [14], [15], [16], [20], [21], [22], [23], [24], [25]. We believe that the increase in SBF may help in accelerating the healing process and the prevention of DFU.

Contrary to our expectation, the study results did not meet our first hypothesis; there was no significant increase in SBF in the calf area and foot area in good glycemic control than in poor glycemic control diabetics. On the other hand, the results from this study supported our second hypothesis; SBF in the calf area was significantly increased more than the foot area in both the good glycemic control and the poor glycemic control diabetics as a result of passive vibration.

In this study, mean foot SBF was higher than the calf at baseline, immediately after vibration and 10 minutes post rest in both good glycemic control and poor glycemic control. One possible explanation could be that the arteriolar myogenic response, vasoarteriolar reflex and precapillary arteriolar vasomotion in the microcirculation are impaired. Normally, all these mechanisms regulate the blood flow during daily

physiological stimuli such as local tissue metabolic needs and positional changes (upright position). Upright position increases hydrostatic pressure in the leg that triggers sensors in the vein to signal the arterioles to constrict. This phenomenon prevents excessive perfusion in the capillaries and the subsequent hypertension. This very important mechanism is deficient in both type 1 and type 2 diabetics (hemodynamic hypothesis) [26]. This could be the reason why we observed higher mean SBF, over time, in foot than calf in both good glycemic control and poor glycemic control diabetics. This could also possibly explain why there was no significant change in foot SBF overtime due to passive vibration in both good glycemic control and poor glycemic control diabetics.

Precapillary arteriolar vasomotion is a phenomenon in which tissues show a rhythmic, slow-wave and high amplitude changes in the arteriolar diameter. This maintains the distribution of blood flowing through capillaries. Failure of this mechanism may fill capillaries permanently and allows no further reserve when the demand is increased. This function is impaired in many pathological conditions such as hyperinsulinaemia (diabetes) [26]. In this study, the percent change in calf SBF from baseline to post vibration was significantly higher in poor glycemic control (132.6%) than good glycemic control (76%) diabetics. There could be two possible explanations for this finding. The possible explanation could be the absence of vasomotion due to hyperinsulinaemia might be higher in poor glycemic control than good glycemic control diabetics. This could be the reason why we observed higher percent change in the calf area in poor glycemic control than in good glycemic control diabetics. On the other hand, the absence of vasomotion is more common in foot than calf. This suggests that calf SBF

in poor glycemic control might have responded well with the passive vibration. Further studies have to be done to analyze this phenomenon.

The mean SBF in calf was almost doubled from baseline (38.9 flux) to immediately after vibration (69.5 flux) in good control control and was more than doubled from baseline (32.9 flux) to immediately after vibration (77.9 flux) in poor glycemic control diabetics. This implies that passive vibration was effective in increasing SBF in calf in both good glycemic control and poor glycemic control diabetics. However, no considerable change in the calf SBF was observed from immediately after vibration to 10 minutes post rest in both good glycemic control and poor glycemic control diabetics. This finding suggests that effect of passive vibration was maintained more than ten minutes after the intervention.

Although significant SBF changes have been documented in the calf, PV for 10 minutes did not significantly increase skin blood flow in the foot; a common site of diabetic ulcers. The percent change of foot SBF from baseline to immediately after vibration was significantly higher in the good glycemic control (72.3%) as compared to the poor glycemic control (32.1%) diabetics. Hyperinsulinaemia and associated impaired vasomotion could be a possible reason why good glycemic control diabetics showed higher calf SBF than the poor glycemic control diabetics. However, from a clinical perspective, distribution of blood in the whole foot is an important factor although the quantity of blood flow is less in micro-vascular bed [(26)]. Therefore, a 72.3% increase in the good glycemic control foot SBF and 32.1% increase in the poor glycemic control foot SBF imply that passive vibration to the foot in both good glycemic control and poor

glycemic control diabetics can be a good "head start" in maintaining healthy circulation in foot.

In our study, we tried to minimize all the external factors that could mask the effect of passive vibration. However, we did not stop the subjects from taking their blood pressure and glucose control medications such as diuretics and metformin from a clinical perspective. These medications could lower blood pressure [27] and might have masked the effect of passive vibration. High fat meal also decreases blood flow [28] and may have masked the vibration's effect if subjects had high fat meal before vibration. Future studies should focus on comparing the effect of vibration with and without high fat meal prior to vibration. We did not record the subject's physical activity just prior to the vibration application although we recorded their general physical activity. Exercising before vibration can increase or decrease the skin blood flow based on the training activity [29] and thus may mask the effect of passive vibration. All of these factors could have masked the real effect of passive vibration and can be avoided in the future studies. Future studies can also examine whether assessing blood flow in the whole foot rather than a single point for at least one minute. This would be helpful in understanding the blood distribution in the micro-vascular bed.

Conclusion

Findings of higher mean calf SBF overtime in both poor glycemic control and good glycemic control, higher percent change of calf SBF from baseline to immediately after vibration in poor glycemic control than good glycemic control and higher percent change of foot SBF from baseline to immediately after vibration in good glycemic

control than poor glycemic control suggest that passive vibration can be safely applied to maintain good circulation in the lower extremities. Although the observed increase in foot was less in poor glycemic control, the distribution not the quantity plays a vital part in the micro-vascular bed.

Acknowledgement

Gurinder S. Bains, Kulbhushan H. Dhamane, Kinjal J. Solani for their immense help in collecting data.

References

1. Centers for Disease Control and Prevention. National diabetes fact sheet: national estimates and general information on diabetes and prediabetes in the United States, 2011. Atlanta, GA: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, 2011.

2. Ziegler D. Diabetic cardiovascular autonomic neuropathy: prognosis, diagnosis and treatment. Diabetes Metab Rev. 1994 Dec;10(4):339-83.

3. Sumpio BE. Foot ulcers. New Engl J Med. 2000 Sep 14;343(11):787-93.

4. Hartemann-Heurtier A, Sultan S, Sachon C, Bosquet F, Grimaldi A. How type 1 diabetic patients with good or poor glycemic control cope with diabetes-related stress. Diabetes Metab. 2001 Nov;27(5):553-9.

5. Juarez DT, Sentell T, Tokumaru S, Goo R, Dawis JW, Mau MM. Factors asscoiated with poor glycemic control or wide glycemic variability among diabetes patients in Hawaii, 2006-2009; 6: Available from: http://dx.doi.org/10.5888/pcd9.120065.

6. Petrofsky J, Lee S. The effects of type 2 diabetes and aging on vascular endothelial and autonomic function. Med Sci Monit. 2005 Jun;11(6):CR247-54.

7. Berne RM, Levy MN. Principles of Physiology. 4 ed. St. Louis, MO: Mosby; 2005.

8. Petrofsky JS. Resting blood flow in the skin: does it exist, and what is the influence of temperature, aging, and diabetes? J Diabetes Sci Technol. 2012 May;6(3):674-85.

9. Ray CA, Monahan KD. Aging attenuates the vestibulosympathetic reflex in humans. Circulation. 2002 Feb 26;105(8):956-61.

10. Petrofsky JS, Alshammari F, Bains G, Khowailed IA, Lee H, Kuderu YN, et al. What is More Damaging to Vascular Endothelial Function: Diabetes, Age, High BMI, or all of the above? (in press). 2013.

11. Rendell MS, Milliken BK, Finnegan MF, Finney DA, Healy JC. The skin blood flow response in wound healing. Microvasc Res. 1997 May;53(3):222-34.

12. Zweifach BW, Lipowsky HH. Pressure-flow relations in blood and lymph microcirculation. In: Renkin EM, Michel CC, Geiger SR, editors. Handbook of Physiology The Cardiovascualr System. Oxford: Oxford Univ; 1987. p. 251-308.

13. Johnson JM, Brengelmann GL, Hales JR, Vanhoutte PM, Wenger CB. Regulation of the cutaneous circulation. Fed Proc. 1986 Dec;45(13):2841-50.

14. Lohman EB, 3rd, Bains GS, Lohman T, DeLeon M, Petrofsky JS. A comparison of the effect of a variety of thermal and vibratory modalities on skin temperature and blood flow in healthy volunteers. Med Sci Monit. 2011 Sep;17(9):MT72-81.

15. Lohman EB, Sackiriyas KSB, Bains G, Calandra G, Lobo C, Nakhro D, et al. A comparison of whole body vibration and moist heat on lower extremity skin temperature and skin blood flow in healthy older individuals. Med Sci Monit. 2012;18(7):CR415-24.

16. Lohman EB, 3rd, Petrofsky JS, Maloney-Hinds C, Betts-Schwab H, Thorpe D. The effect of whole body vibration on lower extremity skin blood flow in normal subjects. Med Sci Monit. 2007 Feb;13(2):CR71-6.

17. Wells PS, Owen C, Doucette S, Fergusson D, Tran HY. Does this patient have deep vein thrombosis? Jama-J Am Med Assoc. 2006 Jan 11;295(2):199-207.

18. SPSS 20.0 for Windows Manual. Chicago, I11: SPSS, Inc; 2013.

19. Donayre CE. Diagnosis and Management of Vascular Ulcers. In: Sussman C, Jensen BM, editors. Wound Care: A colloborative Practice Manual for Physical Therapists and Nurses. Gaithersburg: Aspen publishers, Inc; 1998. p. 301-13.

20. Maloney-Hinds C, Petrofsky JS, Zimmerman G. The effect of 30 Hz vs. 50 Hz passive vibration and duration of vibration on skin blood flow in the arm. Med Sci Monit. 2008 Mar;14(3):CR112-6.

21. Maloney-Hinds C, Petrofsky JS, Zimmerman G, Hessinger DA. The role of nitric oxide in skin blood flow increases due to vibration in healthy adults and adults with type 2 diabetes. Diabetes Technol Ther. 2009 Jan;11(1):39-43.

22. Maikala RV, Bhambhani YN. In vivo lumbar erector spinae oxygenation and blood volume measurements in healthy men during seated whole-body vibration. Exp Physiol. 2006 Sep;91(5):853-66.

23. Bovenzi M, Lindsell CJ, Griffin MJ. Response of finger circulation to energy equivalent combinations of magnitude and duration of vibration. Occup Environ Med. 2001 Mar;58(3):185-93.

24. Stewart JM, Karman C, Montgomery LD, McLeod KJ. Plantar vibration improves leg fluid flow in perimenopausal women. Am J Physiol Regul Integr Comp Physiol. 2005 Mar;288(3):R623-9.

25. Skoglund CR. Vasodilatation in human skin induced by low-amplitude high-frequency vibration. Clin Physiol. 1989 Aug;9(4):361-72.

26. Wiernsperger NF, Bouskela E. Microcirculation in insulin resistance and diabetes: more than just a complication. Diabetes Metab. 2003 Sep;29(4 Pt 2):6S77-87.

27. Giugliano D, De Rosa N, Di Maro G, Marfella R, Acampora R, Buoninconti R, et al. Metformin improves glucose, lipid metabolism, and reduces blood pressure in hypertensive, obese women. Diabetes Care. 1993 Oct;16(10):1387-90.

28. Bui C, Petrofsky J, Berk L, Shavlik D, Remigio W, Montgomery S. Acute effect of a single high-fat meal on forearm blood flow, blood pressure and heart rate in healthy male Asians and Caucasians: a pilot study. Southeast Asian J Trop Med Public Health. 2010 Mar;41(2):490-500.

29. Johnson JM. Physical training and the control of skin blood flow. Med Sci Sports Exerc. 1998 Mar;30(3):382-6.

CHAPTER THREE

EFFECT OF PASSIVE VIBRATION ON SKIN BLOOD FLOW, SKIN TEMPERATURE AND BLOOD PRESSURE IN GOOD GLYCEMIC CONTROL AND POOR GLYCEMIC CONTROL TYPE 2 DIABETICS

Kanikkai Steni Balan Sackiriyas, MPT

Everett B. Lohman, DSc

Noha S. Daher, DrPH

Lee S. Berk, DrPH

Rafael Canizales, PhD

Ernie Schwab, PhD

Dept. of Physical Therapy, School of Allied Health Professions
Loma Linda University, Loma Linda, California, USA

Abstract

Objective

To study the effect of passive vibration on skin blood flow (SBF), skin temperature (ST) and blood pressure (BP) in good glycemic control and poor glycemic control type 2 diabetics.

Materials and Methods

Seventeen good glycemic control (HbA1c < 7.5%) and fifteen poor glycemic control (HbA1c > 9%) type 2 diabetics received passive vibration to their calf and foot on the same day. The SBF, ST and BP were measured before, immediately after vibration and 10 minutes post the vibration application.

Results

There was a significant increase in the mean SBF in the calf from baseline to immediately after vibration in the good glycemic control and the poor glycemic control groups. The mean skin blood flow in the calf almost doubled from baseline (38.8 flux) to immediately after vibration (67.5 flux) and 10 minutes post rest (65.1 flux) in the good glycemic control diabetics (p=.02). The mean SBF in the calf more than doubled from the baseline (31.7 flux) to immediately after vibration (73.4 flux) and 10 minutes post rest (67.6 flux) in the poor glycemic control diabetics (p=.00). However, there was no significant difference in mean foot SBF over time in both good glycemic control and poor glycemic control diabetics. Baseline resting mean of SBF was higher in foot than in calf for both groups of diabetics. The percent change in calf SBF was higher in the poor

glycemic control (131.6%) than the good glycemic control diabetics (71.2%) from baseline to immediately after vibration. However, foot SBF showed higher percent increase in the good glycemic control (91.3%) than the poor glycemic control (32.6%) diabetics from baseline to immediately after vibration. The percent increase was 99.5% in the calf and 63.8% in the foot irrespective of group. There was no clinically significant difference in the mean calf and foot ST and BP in both groups of diabetics.

Conclusion

Based on the results observed in this study, we suggest that passive vibration can be safely administered to the calf area and the foot area without significantly increasing the risk of burns, skin temperature and blood pressure in both good glycemic control and poor glycemic control type 2 diabetics.

Key Words

Good Glycemic Control**,** Poor Glycemic Control, Diabetes Mellitus, Passive Vibration, Skin Circulation, MOOR FLPI, Full-field Laser Perfusion Imager.

ABBREVIATIONS

DM	Diabetes Mellitus
T2D	Type 2 Diabetics
HbA1c	Hemoglobin Assay A1c or Glycohemoglobin
CDC	The Centers for Disease Control and Prevention
BP	Blood Pressure
AVA	Arteriovenous Anastomoses
NUTR	Nutritive
SBF	Skin Blood Flow
BMI	Body Mass Index
NTS	Nucleus Tractus Solitarii
PV	Passive Vibration
ST	Skin Temperature
DVT	Deep Vein Thrombosis
LLU	Loma Linda University
FLPI	Full-field Laser Perfusion Imager
SPSS	Statistical Product and Service Solutions
ml	Milliliter
min	Minute
SBP	Systolic Blood Pressure
PVD	Diastolic Blood Pressure

Introduction

Diabetes Mellitus (DM) is a major health care problem around the world. According to the International Diabetes Federation, 371 million people are living with diabetes around the globe. North America and the Caribbean spent more healthcare dollars on diabetes than any other region in the world. The Unites States of America is the third leading country with 24.1 million diabetics, with China (92.3 M) and India (63.0 M) being the top two countries with diabetes [(1)]. Medical expenses and death rate are two times higher in diabetics than non-diabetics [(2), (3)]. Type 2 diabetes (T2D) is the most common type of diabetes mellitus (90% to 95% of all forms of diabetes) and results from the body's inability to use the circulating insulin although circulating insulin level maybe normal or in some cases elevated [(2), (3), (4)]. Hemoglobin Assay A1c or Glycohemoglobin is a reliable test that reflects the average control of glucose over the past three months [(5)]. According to the Centers for Disease Control and Prevention (CDC), DM can be classified into good glycemic control (HbA1c <7.5%), fair glycemic control (HbA1c ≥7.5% to ≤9%) and poor glycemic control (HbA1c >9%), based on the Hemoglobin A1c (HbA1c) level [(6), (7)].

Circulation

Skin circulation is a highly regulated phenomenon in response to various physical and humoral stimuli [(8)]. It plays a key role in the regulation of temperature [(9)], baroreflex control of blood pressure (BP) [(9)] and tissue healing [(10)]. The central nervous system and the metabolic state of tissues controls the skin circulation [(11)]. The architecture of the micro vascular system is not uniform and varies in glabrous (non hairy) and nonglabrous

(hairy) skin [12]. The glabrous skin (palms, soles, lips, face, tips of fingers and toes) has deeply located numerous thick-walled thermo-regulating arteriovenous anastomoses (AVA) [13]. It is mainly innervated by sympathetic vasoconstrictor nerves [9], [12], [14], [15]. Numerous larger diameter arterioles and venules in these areas allow low resistance, high blood flow directly from the arterioles to venules [9], [12], [16], [17], [18], [19]. In contrast to that, the nonglabrous skin (dorsal area of hand, foot) has more superficial nutritive (NUTR) perfusion through small capillaries with fewer AVA and is controlled by both the sympathetic vasoconstrictor and vasodilator nerves [15], [20]. These differences may lead to differential SBF rates.

Resting skin blood flow in a thermoneutral environment is about 5%-10% of cardiac output (250 mL/min) [9], [21]. This is because of the dominant activity of the vasoconstrictor system in thermoneutral environments [22]. The skin reaches about 50%-70% of cardiac output (6 to 8 L/min) during exercise or heat exposure [9], [21]. The sympathetic vasodilator system is not active during normothermia but activated only during hyperthermia. The larger increase in the skin circulation during hyperthermia is primarily achieved by activation of the sympathetic vasodilator nerves (80%-90%) and to a smaller extent by withdrawal of the sympathetic vasoconstrictor nerves (10%-20%) [15], [23], [9]. Thus, subtle changes in the skin circulation play a crucial role in maintaining the normal human temperature (homeostasis) through heat dissipation (cutaneous vasodilation and sweating) and heat generation [9]. For example, a rise of as little as 8 ml per 100 ml/min over the entire body surface from the neutral level can double the heat transfer to the environment [24].

Aging, body mass index (BMI), and diabetes impair the function of endothelial cells and autonomic nervous system, hence decreases microcirculation [10], [25], [26]. Inabilities of the blood vessels to vasodilate in type 2 diabetes impair the normal heat dissipation and increase the risk of heat exhaustion [9], [27], [28]. Researchers believe SBF has no significant impact on the baroreflex control of BP unlike the skeletal muscles [29]. However, baroreceptor reflex is an important mechanism that rapidly adjusts BP changes. Receptors in the carotid sinus and aortic arch carry the afferent information to the nucleus tractus solitarii (NTS). Short interneurons connect the NTS to the dorsal motor nucleus of the vagus and nucleus ambiquus (parasympathetic efferent), and rostral ventrolateral medulla oblongate (sympathetic efferent). A rise in the BP stimulates the baroreceptors and in turn increases the vagal tone and decreases the sympathetic tone. The opposite happens when there is a decrease in the BP [30]. In recent years, research studies supported the role of sympathetic vasodilator and vasoconstrictor systems in the BP regulation [21], [31], [32], [33], [34]. For example, the skin vasoconstrictor system was active when unloading of baroreceptors was achieved using lower-body negative pressure. However, skin circulation is low in thermoneutral environments. During hyperthermia, the vasodilator system is active and skin receives 50%-70% of cardiac output. Studies show that skin vasoconstricts through withdrawal of the vasodilator system when lower body negative pressure is applied during hyperthermia [21], [32]. This implies that sympathetic activity in skin plays an integrated role in thermoregulation and the regulation of blood pressure. Impairment in one system can affect the other system [9].

In research, the use of passive vibration (PV) to improve skin blood flow (SBF) without increasing the risk of burns has been performed and supported. A series of

studies performed by Lohman et al and Maloney-Hinds et al showed that PV significantly improved SBF in hairy and non-hairy skin in healthy volunteers, healthy older individuals, good to fair glycemic control diabetics and non-diabetics [35], [36], [37], [38], [39], [40]. However, there was no research study examining the effect of PV in increasing SBF in diabetics without affecting skin temperature and blood pressure. The purpose of this study was to examine the effect of PV on SBF, skin temperature (ST) and blood pressure (BP) in good glycemic control versus poor glycemic control diabetics. We hypothesized that SBF in the calf area and the foot area without significantly affecting the skin temperature and blood pressure would be higher in good glycemic control than in poor glycemic control type 2 diabetics as a result of passive vibration.

Material and Methods

Study Population

Type 2 diabetics between the age ranges of 18-75 years were invited to participate in this study. Subjects with neurological disorders, orthopedic disorders, bleeding disorders, leg ulcer, chronically exposed to vibration, cardiovascular diseases, possible deep vein thrombosis (DVT) with a score of 2 (high risk) in well's criteria [41] or pregnant were excluded. Thirty seven subjects were recruited through fliers and word of mouth, and from the Diabetes Support Group and from the Diabetes Treatment Center at Loma Linda University (LLU) Medical Center. Five subjects were excluded because they did not meet the inclusion criteria. All the subjects were assigned to one of two groups: Group 1=Good glycemic control and Group 2=Poor glycemic control. Subjects received passive vibration to their calf and the opposite foot on the same day. All procedures were

approved by the LLU's institutional review board and each subject signed a statement of informed consent (Appendix A).

Instrumentation

A Physio Plate® (Domino S.R.L, San Vendemiano, Italy) was used to deliver passive vibration at a frequency of 50 Hz for a total number of ten cycles (one cycle= 60s working time: 2s rest time) or approximately ten minutes (Figure 9). Skin blood flow was measured non-invasively by using a MOOR Full-field Laser Perfusion Imager **(**FLPI) (MOOR FLPI V 2.1, Oxford, England) that was pre-warmed for about 30 minutes (Figure 10). It uses a red light laser beam (632.8 nm) applied perpendicularly to capture SBF and the blood flow was measured in "Flux" unit. Skin temperatures were measured using a thermistor placed on the muscle belly of posterior calf muscle and on the plantar aspect of the first three metatarsal heads (Figure 11). The thermistor was manufactured by BioPac systems (BioPac Inc., Goleta, CA) and the output was sensed by an SKT 100 thermistor amplifier. This analog data was converted into a digital data by the BioPac systems (BioPac Inc., Goleta, CA). A mean temperature was taken to analyze the data. Blood pressure at the brachial artery was measured using a blood pressure cuff monitor (RITE AID, Camp Hill, PA) (Figure 12).

Figure 9. Physio Plate® vibration platform.

Figure 10. MOOR FLPI.

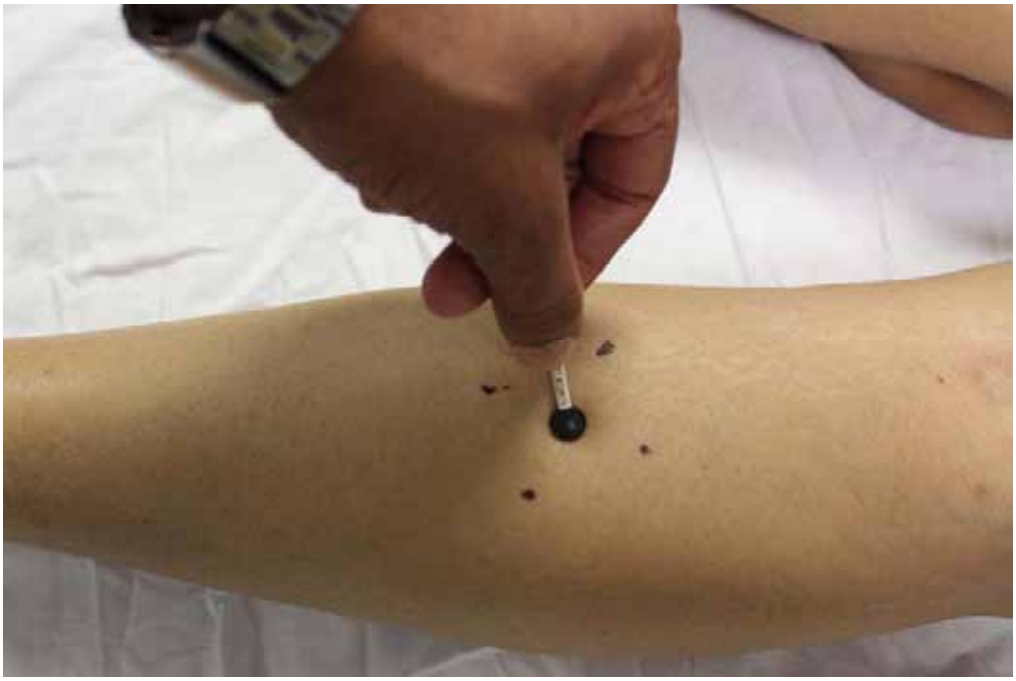


Figure 11. Thermistor.

Figure 12. Blood pressure measurement.

Procedure

Screening

The testing room temperature was maintained between 71.6°F-75.2°F (22°-24° C) for about 30 minutes before the subjects enters. Subjects were asked to take rest in supine position for about 30 minutes to stabilize their blood flow before intervention. Subjects were screened for exclusion and demographic data was collected (Appendix B).

Cutaneous sensation was assessed using a Semmes-Weinstein Monofilament (North Coast Medical, Inc, Morgan Hill, CA, USA) and the response, color of the handle and notations were noted on the sensory foot mapping form (Appendix C). Vibration sense was assessed using a 128 Hz tuning fork and subjects with a score of 2 (absent sensation) were excluded.

Testing

A square shaped 3 cm x 3 cm area was marked on the posterior aspect of the calf (muscle belly) and on the plantar aspect of the first three (1-3) metatarsal heads while the subjects were in prone position on a plinth. Baseline SBF, ST and BP was measured. Then, subjects received passive vibration to their calf for about ten minutes (Figure 13). The second reading was taken immediately after vibration. Subjects were given a ten minutes rest before the third reading was taken. The same procedures were repeated for foot on the opposite leg (Figure 14).

Figure 13. Calf area vibration.

Figure 14. Foot area vibration.

Data Analysis

Data was analyzed using SPSS version 20.0 [42]. The distributions of the continuous variables were examined using one sample Kolmogorov Smirnov test. The proportions of males & females, ethnicity and levels of physical activity by group were compared using chi-square test of independence. We compared mean age and body mass index (BMI) by group using independent t-test. Mixed factorial analysis of variance was used to compare the effect of passive vibration on SBF, ST and BP from baseline to post vibration and 10 minutes post rest in good glycemic control and poor glycemic control Type 2 diabetic subjects' calf and foot. Significant differences were further examined with Bonferroni test. The level of significance was set at $p<.05$.

Results

Seventeen good and fifteen poor glycemic control type 2 diabetics participated in this study. The results of the Kolmogorov Smirnov test showed that the distribution of age, BMI and SBF were approximately normal. Results showed that there were no significant differences between the good glycemic control and poor glycemic control diabetics in terms of gender, race, physical activity, age and BMI ($p>.05$) (Table 3).

Table 3. Distribution of demographic data by group (N=32).

Variables		Good (n=17)	Poor (n=15)	p-value
Gender†	Male	10 (58.8%)	7 (41.2%)	.49
	Female	7 (46.7%)	8 (53.3%)	
Ethnicity†	White	7 (63.6%)	4 (36.4%)	.37
	Others¶	3 (30%)	7 (70%)	
	Hispanic	4 (66.7%)	2 (33.3%)	
	African American	3 (60%)	2 (40%)	
Physical activity†	Very light	3 (30%)	7 (70%)	.15
	Light	6 (75%)	2 (25%)	
	Moderate & Heavy	8 (57.1%)	6 (42.9%)	
Age (Mean±SD)*		61.5±11.5	56.1±7.2	.12
BMI (Mean±SD)*		30.7±5.6	32.3±6.5	.47

†: Chi-square test

*: Independent t test

¶: Others: Asians, Middle eastern

Skin Blood Flow

Good Glycemic Control

A significant change in mean calf SBF was observed over time in good glycemic control diabetics ($F_{2, 32}$=6.53, p=.02) (Table 4). A significant change was detected between baseline and immediately after vibration (p=.03) and between baseline and 10 minutes post rest (p=.03). However, the mean foot SBF did not significantly changed over time in good glycemic control diabetics ($F_{2, 32}$=2.9, p=.09). The mean SBF was significantly higher in foot than in calf in the good glycemic control at baseline

(130.4±22.2 vs 38.8±2.2; p<.01), immediately after vibration (181.0±28.0 vs 67.5±12.0; p<.001) and 10 minutes post rest (139.3±20.6 vs 65.1±11.0; p<.01) (Figure 15).

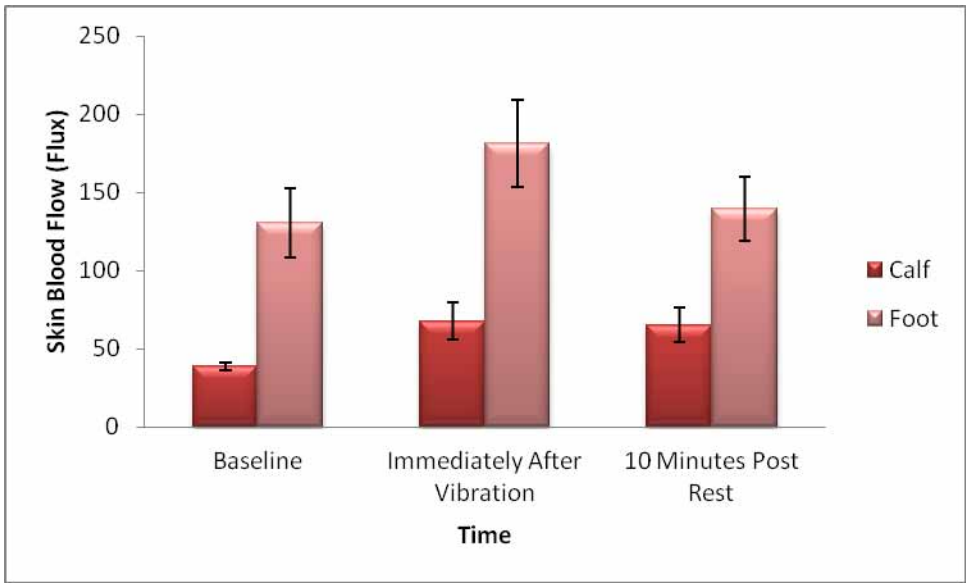


Figure 15. Changes in mean±SE† SBF† by site in good glycemic control diabetics over time.

†SBF: Skin blood flow

†SE: Standard error

Poor Glycemic Control

A significant change in mean calf SBF was observed over time in poor control diabetics ($F_{2, 28}$=12.1, p=.01) (Table 4). A Significant change was observed between baseline and immediately after passive vibration (p=.01) and between baseline and 10 minutes post rest (p=.01). There was no significant change in mean foot SBF over time in poor glycemic control diabetics ($F_{2, 28}$=.07, p=.86). The mean SBF was significantly higher in foot than in calf in poor glycemic control at baseline (140.0±28.6 vs 31.7±2.3;

p<.01), immediately after vibration (146.9±27.8 73.4±12.7; p=.03) and 10 minutes post rest (145.1±31.0 vs 67.6±10.5; p=.03) (Figure 16).

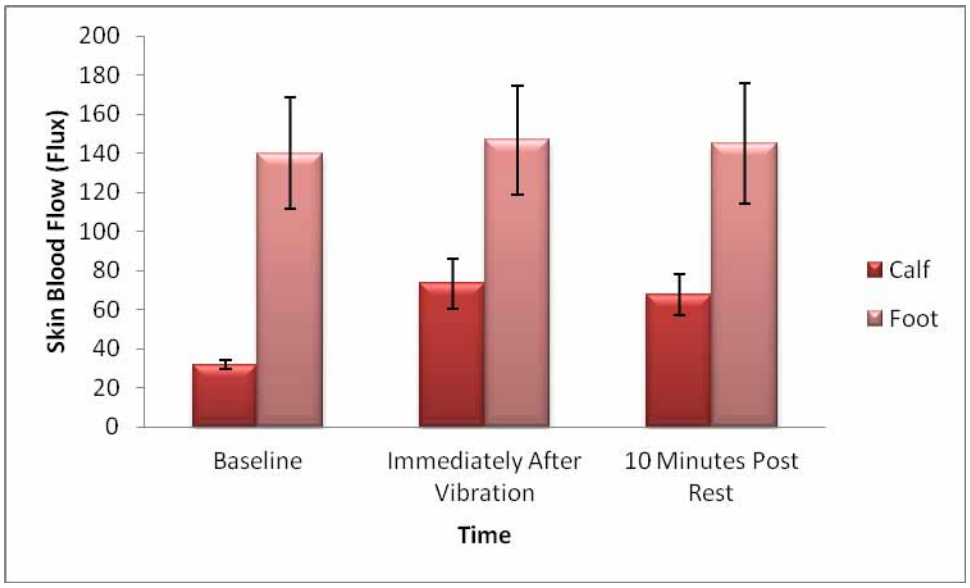


Figure 16. Changes in mean±SE† SBF† by site in poor glycemic control diabetics over time.

†SBF: Skin blood flow

†SE: Standard error

Table 4. Mean (SE†) skin blood flow over time by group and site.

Site	Group	Baseline	Immediately after vibration	10 min post rest	p-value*
Calf	**Good**	38.8(2.20)	67.5(12.0)	65.1(11.0)	.02
	Poor	31.7(2.3)	73.4(12.7)	67.6(10.5)	<.01
Foot	**Good**	130.4(22.2)	181.0(28.0)	139.3(20.6)	.09
	Poor	140.0(28.6)	146.9(27.8)	145.1(31.0)	.86

*Analysis of variance
†SE: Standard error

Good Glycemic Control vs. Poor Glycemic Control

There was a significant difference in mean calf SBF over time in both good and poor glycemic control diabetics ($F_{2, 60}$=18.20, p<.001). Based on the Bonferroni test, there was a significant difference in calf SBF between baseline and immediately after vibration (p<.001) and between baseline and 10 minutes post rest (p<.001) in both good glycemic control and poor glycemic control diabetics. There was no significant interaction between calf SBF and group ($F_{2, 60}$=.56, p=.49). In addition, there was no significant difference between groups ($F_{1, 30}$=.01, p=.97). There was no significant difference in mean calf SBF between immediately after vibration and 10 minutes post rest (p=.40). There was no significant difference in foot SBF over time in both good glycemic control and poor glycemic control diabetics ($F_{2, 60}$=2.0, p=.16). There was no significant interaction between foot SBF and group ($F_{2, 60}$=1.31, p=.27). Also, there was no significant difference in mean foot SBF between groups ($F_{1, 30}$=.04, p=.85).

Good Glycemic Control

There was no significant change in mean calf ST over time in good glycemic control diabetics ($F_{2, 32}$=0.53, p=.50) (Table 5). However, a significant change was detected in mean foot ST over time in good glycemic control diabetics ($F_{2, 32}$=6.1, p<.01). There was a significant change detected between baseline and immediately after vibration (p=.02), and between immediately after vibration and 10 minutes post rest (p=.04). There was a significant difference in mean ST between calf and foot in good glycemic control diabetics at baseline (t_{16}=5.2, p<.001), immediately after vibration (t_{16}=4.8, p<.001) and 10 minutes post rest (t_{16}=5.5, p<.001). The mean ST in the good glycemic control was significantly higher in calf than in foot at baseline (88.5±0.8 vs 84.2±0.7; p<.001), immediately after vibration (88.6±0.3 vs 85.6±0.6; p<.001) and 10 minutes post rest (87.9±0.4 vs 84.6±0.7; p<.001) (Figure 17).

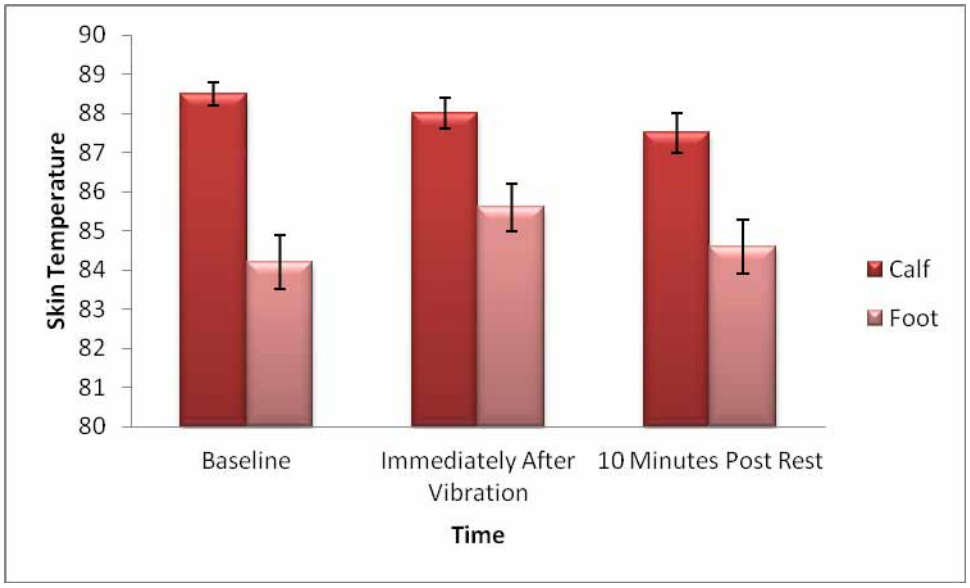


Figure 17. Changes in mean±SE† ST† by site in good glycemic control diabetics over time .

†SE: Standard error

†ST: Skin temperature

Poor Glycemic Control

There was no significant change in mean calf ST over time in poor glycemic control diabetics ($F_{2, 28}$=2.2, p=.13) (Table 5). Also, there was no significant change in mean foot ST over time in poor glycemic control diabetics ($F_{2, 28}$=2.5, p=.10). However, there was a significant difference in mean ST between calf and foot in the poor glycemic control diabetics at baseline (t_{14}=3.4, p<.01), immediately after vibration (t_{14}=2.7, p=.02), and 10 minutes post rest (t_{14}=3.1, p=.01). The mean ST in the good glycemic control was significantly higher in calf than in foot at baseline (87.3±0.3 vs 84.8±0.8; p<.01), immediately after vibration (88.0±0.4 vs 86.2±0.8; p=.02), and 10 minutes post rest (87.5±0.5 vs 85.4±0.7; p<.01) (Figure 18).

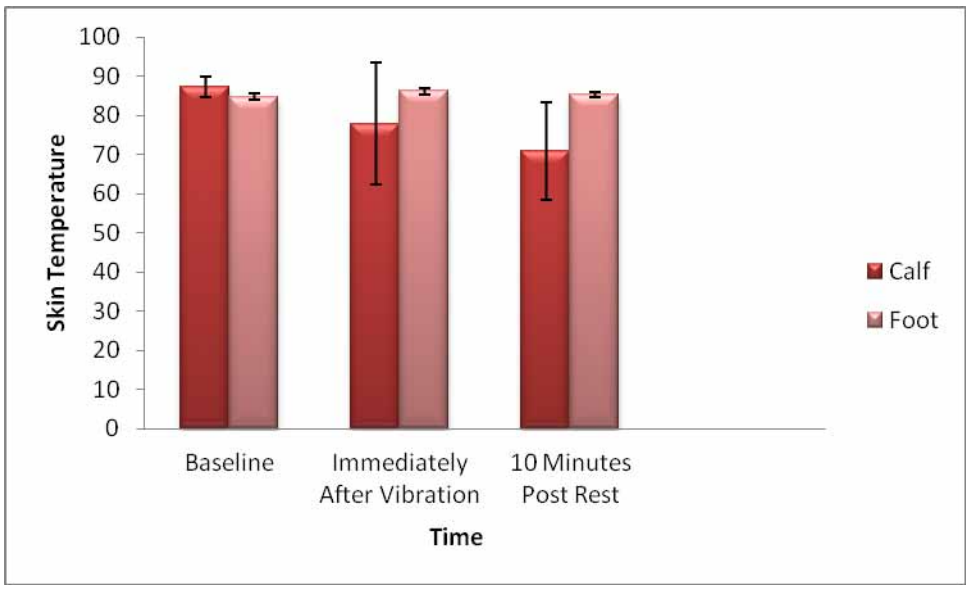


Figure 18. Changes in mean±SE† ST† by site in poor glycemic control diabetics.

†SE: Standard error

†ST: Skin temperature

Table 5. Mean (SE†) skin temperature over time by group and site.

Site	Group	Baseline	Immediately after vibration	10 min post rest	p-value*
Calf	**Good**	88.5(0.3)	88.0(0.4)	87.5(0.5)	.50
	Poor	87.3(2.6)	77.9(15.5)	70.9(12.5)	.13
Foot	**Good**	84.2(0.7)	85.6(0.6)	84.6(0.7)	<.01
	Poor	84.8(0.8)	86.2(0.8)	85.4(0.7)	.10

*Analysis of variance
†SE: Standard error

Good Glycemic Control vs. Poor Glycemic Control

There was no significant difference in mean calf ST over time in both good glycemic control and poor glycemic control diabetics ($F_{2, 60}$=1.11, p=.31). Also, there was no significant interaction between group and calf temperature ($F_{2, 60}$=0.45, p=.55). There was no significant difference between groups ($F_{1, 30}$=1.79, p=.19). However, there was a significant difference in mean foot ST over time in both good glycemic control and poor glycemic control over time ($F_{2, 60}$=7.3, p=.001). Based on the Bonferroni test, there was a significant difference in foot ST between baseline and immediately after vibration (p=.002) and between immediately after vibration and 10 minutes post rest (p=.04) in both good glycemic control and poor glycemic control diabetics. There was no significant interaction between foot ST and group ($F_{2, 60}$=0.07, p=.93). There was no significant difference in mean foot ST between groups ($F_{1, 30}$=.54, p=.47).

Blood Pressure

Systolic Blood Pressure

Good Glycemic Control

There was no significant change in mean systolic blood pressure (SBP) over time during calf vibration in good glycemic control diabetics ($F_{2, 32}$=4.2, p=.06) (Table 6). There was no significant change in mean SBP over time during foot vibration in good glycemic control diabetics ($F_{2, 32}$=.8, p=.44). There was a significant difference in mean SBP between calf and foot in the good glycemic control diabetics at immediately after vibration (p=.01). However, there was no significant difference in mean SBP between

calf and foot in the good glycemic control at baseline (p=.23) and 10 minutes post rest (p=.1).

Poor Glycemic Control

There was no significant change in mean SBP over time during calf vibration in poor glycemic control diabetics ($F_{2, 28}$=.5, p=.54) (Table 6). There was no significant change in mean SBP over time during foot vibration in poor glycemic control diabetics ($F_{2, 28}$=.2, p=.76). There was no significant difference in mean SBP between calf and foot in the good glycemic control diabetics at baseline (p=.83), immediately after vibration (p=.65) and 10 minutes post rest (p=.13).

Table 6. Mean (SE†) systolic blood pressure over time by group and site.

Site	Group	Baseline	Immediately after vibration	10 min post rest	p-value*
Calf	**Good**	124.7(2.4)	131.8(4.5)	128.5(3.4)	.06
	Poor	128.1(3.2)	128.7(4.7)	131.3(3.4)	.54
Foot	**Good**	122.5(2.3)	124.9(3.3)	124.7(2.4)	.44
	Poor	127.7(4.0)	126.7(2.8)	128.1(3.2)	.76

*Analysis of variance
†SE: Standard error

Good Glycemic Control vs. Poor Glycemic Control

There was no significant difference in mean calf SBP over time in both good glycemic control and poor glycemic control diabetics ($F_{2, 60}$=2.1, p=.15). Also, there was

no significant interaction between group and calf SBP ($F_{2, 60}$=1.5, p=.23). There was no significant difference between groups ($F_{1, 30}$=.1, p=.82). There was no significant difference in mean foot SBP over time in both good glycemic control and poor glycemic control diabetics ($F_{2, 60}$=.3, p=.67). There was no significant interaction between foot SBP and group ($F_{2, 60}$=.5, p=.54). There was no significant difference in mean foot SBP between groups ($F_{1, 30}$=.8, p=.37).

Diastolic Blood Pressure

Good Glycemic Control

There was no significant change in mean diastolic blood pressure (DBP) over time during calf vibration in good glycemic control diabetics ($F_{2, 32}$=.9, p=.34) (Table 7). There was no significant change in mean DBP over time during foot vibration in good glycemic control diabetics ($F_{2, 32}$=5.5, p=.39). There was no significant difference in mean DBP between calf and foot in the good glycemic control at baseline (p=.53), immediately after vibration (p=.29) and 10 minutes post rest (p=.36).

Poor Glycemic Control

There was no significant change in mean DBP over time during calf vibration in poor glycemic control diabetics ($F_{2, 28}$=4.8, p=.05) (Tabel 7). There was no significant change in mean DBP over time during foot vibration in poor glycemic control diabetics ($F_{2, 28}$=1.0, p=.37). There was no significant difference in mean DBP between calf and foot in the poor glycemic control diabetics at baseline (p=.11) and immediately after vibration (p=.50). However, there was a significant difference between calf and foot at 10 minutes post rest (p=.02) (Figure 2).

Table 7. Mean (SE†) diastolic blood pressure over time by group and site.

Site	Group	Baseline	Immediately after vibration	10 min post rest	p-value*
Calf	**Good**	74.1(1.7)	75.8(1.8)	75.6(1.5)	.43
	Poor	79.6(1.8)	78.7(1.4)	83.3(1.8)	.05
Foot	**Good**	73.2(1.2)	74.2(1.4)	74.1(1.7)	.39
	Poor	77.7(2.0)	80.1(1.7)	79.6(1.8)	.37

*Analysis of variance
†SE: Standard error

Good Glycemic Control vs. Poor Glycemic Control

There was no significant difference in mean calf DBP over time in both good glycemic control and poor glycemic control diabetics ($F_{2, 60}$=3.4, p=.07). Also, there was no significant interaction between group and calf DBP ($F_{2, 60}$=2.6, p=.08). However, there was a significant difference between groups ($F_{1, 30}$=7.2, p=.01). There was no significant difference in mean foot DBP over time in both good glycemic control and poor glycemic control diabetics ($F_{2, 60}$=1.4, p=.26). There was no significant interaction between foot DBP and group ($F_{2, 60}$=.2, p=.83). However, there was a significant difference in mean foot DBP between groups ($F_{1, 30}$=7.4, p=.01).

Discussion

Body temperature, skin blood flow (SBF) and blood pressure (BP) measurements can provide important information about the status of the cardiovascular and thermoregulatory systems. They provide the body's physiological status and their

response to various stimuli such as physical activity, stress and environmental influences [43]. Studies from the Department of Physical Therapy in the Loma Linda University and others have shown that vibration can be effective in increasing SBF in diabetics as well as in non-diabetics [38], [36], [37], [35], [39], [44], [45], [46], [47].

Results of this study showed that the mean SBF in the hairy skin (calf) was improved in both good glycemic control and poor glycemic control diabetics. This improvement was detected from baseline to immediately after vibration, and from baseline to 10 minutes post vibration intervention with no significant increase in the ST and SBF. There was a significant difference in the mean DBP between the groups. However, the mean difference is 5.3 mm of Hg and can be considered clinically not significant. The increase in mean calf SBF was almost doubled between baselines (38.8) to immediately after vibration (67.5) and to 10 minutes post rest (65.1) in the good glycemic control diabetics. The increase in mean calf SBF was more than doubled from baseline (31.7) to immediately after vibration (73.4) and to 10 minutes post rest (67.6) in the poor glycemic control diabetics. However, the percent change in calf SBF was higher in the poor glycemic control (131.6%) than the good glycemic control diabetics (71.2%) between baseline to immediately after vibration. No significant difference in the mean calf SBF between immediately after vibration to 10 minutes post rest in both the groups were detected, suggesting that both groups responded to passive vibration similarly. The calf SBF remained elevated at ten minutes post PV and was beginning to decline in both the groups.

In contrast to the hairy skin (calf), the foot (non hairy) showed no significant increase in mean SBF across time in and between both good glycemic control and poor

glycemic control diabetics. However, the highest percent change in the foot SBF was seen in good glycemic control (91.3%) as compared to poor glycemic control (32.6%). Although the percent change is less in poor glycemic control, we agree with Wiernsperger and Bouskela that distribution of blood in the microvascular bed is the primary factor and not the quantity [8]. The foot of the good glycemic control diabetics showed a mean temperature difference of 1.2°F. A mean temperature change of 1.2°F was not considered clinically significant although it was statistically significant. We did not notice any clinically significant rise or fall in the mean systolic and diastolic blood pressure in both groups.

These findings suggest that passive vibration can be used to improve SBF in the calf and foot without the risk of increasing skin burns, heat exhaustion and cardiovascular stress in both good glycemic control and poor glycemic control type 2 diabetics.

Conclusion

Based on the findings, we suggest that passive vibration can be safely administered to calf and foot without increasing the risk of burns; heat exhaustion and increase in blood pressure in both good glycemic control and poor glycemic control type 2 diabetics.

Acknowledgement

Gurinder S. Bains, Kulbhushan H. Dhamane, Kinjal J. Solani, Gabriel Pacheco, Drasti Shah, Brijesh Singh, Samia Algabbani, Charmi Desai, and Fumiaki Isshiki for their immense help in collecting data.

References

1. Diabetes Atlas. 2012; Available from: http://www.idf.org/diabetesatlas/.

2. Centers for Disease Control and Prevention. National diabetes fact sheet: national estimates and general information on diabetes and prediabetes in the United States, 2011. Atlanta, GA: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, 2011.

3. Ziegler D. Diabetic cardiovascular autonomic neuropathy: prognosis, diagnosis and treatment. Diabetes Metab Rev. 1994 Dec;10(4):339-83.

4. Sumpio BE. Foot ulcers. New Engl J Med. 2000 Sep 14;343(11):787-93.

5. National Diabetes Clearinghouse. (January 22, 2013). Insulin Resistance and Prediabetes. Retrieved March 22, 2013 from http://diabetes.niddk.nih.gov/dm/pubs/insulinresistance/index.aspx.

6. Hartemann-Heurtier A, Sultan S, Sachon C, Bosquet F, Grimaldi A. How type 1 diabetic patients with good or poor glycemic control cope with diabetes-related stress. Diabetes Metab. 2001 Nov;27(5):553-9.

7. Juarez DT, Sentell T, Tokumaru S, Goo R, Dawis JW, Mau MM. Factors asscoiated with poor glycemic control or wide glycemic variability among diabetes patients in Hawaii, 2006-2009; 6: Available from: http://dx.doi.org/10.5888/pcd9.120065.

8. Wiernsperger NF, Bouskela E. Microcirculation in insulin resistance and diabetes: more than just a complication. Diabetes Metab. 2003 Sep;29(4 Pt 2):6S77-87.

9. Charkoudian N. Skin blood flow in adult human thermoregulation: how it works, when it does not, and why. Mayo Clin Proc. 2003 May;78(5):603-12.

10. Petrofsky J, Lee S. The effects of type 2 diabetes and aging on vascular endothelial and autonomic function. Med Sci Monit. 2005 Jun;11(6):CR247-54.

11. Berne RM, Levy MN. Principles of Physiology. 4 ed. St. Louis, MO: Mosby; 2005.

12. Rendell MS, Milliken BK, Finnegan MF, Finney DA, Healy JC. The skin blood flow response in wound healing. Microvasc Res. 1997 May;53(3):222-34.

13. Bornmyr S, Svensson H, Lilja B, Sundkvist G. Skin temperature changes and changes in skin blood flow monitored with laser Doppler flowmetry and imaging: a methodological study in normal humans. Clin Physiol. 1997 Jan;17(1):71-81.

14. Lossius K, Eriksen M, Walloe L. Fluctuations in blood flow to acral skin in humans: connection with heart rate and blood pressure variability. J Physiol. 1993 Jan;460:641-55.

15. Johnson JM, Proppe DW. Cardiovascular adjustments to heat stress. In: Fregly MJ, Blatteis CM, editors. Handbook of Physiology: Oxford University Press; 1996. p. 215-43.

16. Hales JR, Jessen C, Fawcett AA, King RB. Skin AVA and capillary dilatation and constriction induced by local skin heating. Pflugers Arch. 1985 Jul;404(3):203-7.

17. Popoff N. The digital vascular system. Arch Pathol. 1934;18:295-330.

18. Rowell LB. Reflex control of the cutaneous vasculature. J Invest Dermatol. 1977 Jul;69(1):154-66.

19. Zweifach BW, Lipowsky HH. Pressure-flow relations in blood and lymph microcirculation. In: Renkin EM, Michel CC, Geiger SR, editors. Handbook of Physiology The Cardiovascualr System. Oxford: Oxford Univ; 1987. p. 251-308.

20. Johnson JM, Brengelmann GL, Hales JR, Vanhoutte PM, Wenger CB. Regulation of the cutaneous circulation. Fed Proc. 1986 Dec;45(13):2841-50.

21. Crandall CG, Johnson JM, Kosiba WA, Kellogg DL, Jr. Baroreceptor control of the cutaneous active vasodilator system. J Appl Physiol. 1996 Nov;81(5):2192-8.

22. Pergola PE, Kellogg DL, Jr., Johnson JM, Kosiba WA. Reflex control of active cutaneous vasodilation by skin temperature in humans. Am J Physiol. 1994 May;266(5 Pt 2):H1979-84.

23. Rowell LB. Cardiovascular aspects of human thermoregulation. Circ Res. 1983 Apr;52(4):367-79.

24. Savage MV, Brengelmann GL. Control of skin blood flow in the neutral zone of human body temperature regulation. J Appl Physiol. 1996 Apr;80(4):1249-57.

25. Ray CA, Monahan KD. Aging attenuates the vestibulosympathetic reflex in humans. Circulation. 2002 Feb 26;105(8):956-61.

26. Petrofsky JS, Alshammari F, Bains G, Khowailed IA, Lee H, Kuderu YN, et al. What is More Damaging to Vascular Endothelial Function: Diabetes, Age, High BMI, or all of the above? (in press). 2013.

27. Schuman SH. Patterns of urban heat-wave deaths and implications for prevention: data from New York and St. Louis during July, 1966. Environ Res. 1972 Mar;5(1):59-75.

28. Semenza JC, McCullough JE, Flanders WD, McGeehin MA, Lumpkin JR. Excess hospital admissions during the July 1995 heat wave in Chicago. Am J Prev Med. 1999 May;16(4):269-77.

29. Wallin BG, Sundlof G, Delius W. The effect of carotid sinus nerve stimulation on muscle and skin nerve sympathetic activity in man. Pflugers Arch. 1975 Jul 21;358(2):101-10.

30. Niederhoffer N, Hein L, Starke K. Modulation of the baroreceptor reflex by alpha 2A-adrenoceptors: a study in alpha 2A knockout mice. Br J Pharmacol. 2004 Mar;141(5):851-9.

31. Johnson JM. Nonthermoregulatory control of human skin blood flow. J Appl Physiol. 1986 Nov;61(5):1613-22.

32. Kellogg DL, Jr., Johnson JM, Kosiba WA. Baroreflex control of the cutaneous active vasodilator system in humans. Circ Res. 1990 May;66(5):1420-6.

33. Rowell LB, Wyss CR, Brengelmann GL. Sustained human skin and muscle vasoconstriction with reduced baroreceptor activity. J Appl Physiol. 1973 May;34(5):639-43.

34. Tripathi A, Nadel ER. Forearm skin and muscle vasoconstriction during lower body negative pressure. J Appl Physiol. 1986 May;60(5):1535-41.

35. Maloney-Hinds C, Petrofsky JS, Zimmerman G. The effect of 30 Hz vs. 50 Hz passive vibration and duration of vibration on skin blood flow in the arm. Med Sci Monit. 2008 Mar;14(3):CR112-6.

36. Lohman EB, 3rd, Bains GS, Lohman T, DeLeon M, Petrofsky JS. A comparison of the effect of a variety of thermal and vibratory modalities on skin temperature and blood flow in healthy volunteers. Med Sci Monit. 2011 Sep;17(9):MT72-81.

37. Lohman EB, Sackiriyas KSB, Bains G, Calandra G, Lobo C, Nakhro D, et al. A comparison of whole body vibration and moist heat on lower extremity skin temperature and skin blood flow in healthy older individuals. Med Sci Monit. 2012;18(7):CR415-24.

38. Lohman EB, 3rd, Petrofsky JS, Maloney-Hinds C, Betts-Schwab H, Thorpe D. The effect of whole body vibration on lower extremity skin blood flow in normal subjects. Med Sci Monit. 2007 Feb;13(2):CR71-6.

39. Maloney-Hinds C, Petrofsky JS, Zimmerman G, Hessinger DA. The role of nitric oxide in skin blood flow increases due to vibration in healthy adults and adults with type 2 diabetes. Diabetes Technol Ther. 2009 Jan;11(1):39-43.

40. Lohman EB, Sackiriyas KS, Bains G, Dhamane KH, Solani KJ, Raju C, K., et al. Effect of Vibration on Skin Blood Flow in Type 2 Diabetes Mellitus (accepted). ijpot. 2013.

41. Wells PS, Owen C, Doucette S, Fergusson D, Tran HY. Does this patient have deep vein thrombosis? Jama-J Am Med Assoc. 2006 Jan 11;295(2):199-207.

42. SPSS 20.0 for Windows Manual. Chicago, I11: SPSS, Inc; 2013.

43. Schmitz TD. Vital Signs. In: O'Sullivan. S. B. Schmitz TJ, editor. Physical Rehabilitation. 5 ed. Philadelphia: F. A. Davis Company. p. 81-120.

44. Maikala RV, Bhambhani YN. In vivo lumbar erector spinae oxygenation and blood volume measurements in healthy men during seated whole-body vibration. Exp Physiol. 2006 Sep;91(5):853-66.

45. Bovenzi M, Lindsell CJ, Griffin MJ. Response of finger circulation to energy equivalent combinations of magnitude and duration of vibration. Occup Environ Med. 2001 Mar;58(3):185-93.

46. Stewart JM, Karman C, Montgomery LD, McLeod KJ. Plantar vibration improves leg fluid flow in perimenopausal women. Am J Physiol Regul Integr Comp Physiol. 2005 Mar;288(3):R623-9.

47. Skoglund CR. Vasodilatation in human skin induced by low-amplitude high-frequency vibration. Clin Physiol. 1989 Aug;9(4):361-72.

CHAPTER FOUR

SUMMARY

Diabetes Mellitus

Diabetes Mellitus is a group of metabolic disorder resulting from no insulin or decreased insulin production from the pancreas. This can impair carbohydrate, fat and protein metabolism and leads to abnormal glucose levels in the blood stream [(1)]. In some instances, the body ineffectively use insulin produced by the pancreatic cells. This leads to build up of abnormal glucose levels in blood stream instead of being absorbed by body cells. Overtime, the beta cells in the body loses its ability to produce enough insulin for the cells to absorb glucose, leading to insulin resistance [(2)]. Aging and diabetes can damage the autonomic nervous system and the endothelial lining of the blood vessels. These damages reduce the release of vaso dilator substances such as prostacyclin and nitric oxide (NO) [(3), (4)] . As a result, the balance between the vasodilators and vasoconstrictors substances is impaired in the endothelial cells leading to increased vasoconstriction. This reduces the resting skin blood flow [(4)]. One of the important functions of the skin is the regulation of temperature in the human body. Thermoregulation helps to maintain the balance between heat generation and heat dissipation during thermoneutral environment and during hyperthermia. This is achieved by the sympathetic vasodilator and vasoconstrictor systems. The ability to vasodilate is impaired in diabetes. This most likely reduces the ability of the blood vessels to dissipate heat during elevated temperature in the environments [(5)].

Impaired skin microcirculation can lead to decreased nutrients to the epidermis and reduces the exchange of waste products with epidermis. Therefore, damage to micro vascular bed and associated reduction in the skin circulation plays a significant role in the insulin metabolism [6] and rate of wound healing [7].

Vibration

Vibration is an intervention that increases skin blood flow in the healthy and diabetic individuals without increasing the risk of burns. The effect on the human body as a result of vibration, is not only biomechanical but also physiological [8]. Vibration can be delivered parallel to the blood vessels (longitudinal) or lateral to the blood vessels (perpendicular). This can cause shear stress to both the larger and smaller vessels. Increased external pressures as a result of perpendicular vibration can damage endothelial tissues on the blood vessels. One of the important effects of lateral vibration (perpendicular) in small vessels (arterioles, capillaries, venules) is the deformation of the blood vessels. Thus, vibration can change the shape of the blood vessels from circular into more or less elliptical. This change of shape from circular to elliptical can increase total peripheral resistance (TPR).

A study performed by Mester et al., (2006) showed that the TPR was significantly reduced after the application of vibration [8]. Mester et al., (2006) suggested that the decrease in TPR during vibration can be achieved by opening of more capillaries or dilatation of blood vessels or both [8]. Mester et al., (2006) proposed that safety during the application of therapeutic vibration should be considered to avoid various damages that may cause headache, internal bleeding or even death [8]. This can be avoided by

following the guidelines associated with vibration parameters. However, more research studies have to be done to establish guidelines for parameters such as the frequency, amplitude, duration of the each vibration application, resting interval, total duration of the vibration application and position of the body.

Studies form the Department of Physical Therapy

A series of studies have been conducted from the Department of Physical Therapy, Loma Linda University (LLU) to examine the effect of a specific frequency and specific time in improving SBF due to active and passive vibration in healthy, diabetic and non diabetic individuals.

In the first study, forty five healthy subjects aged between 18-43 years participated and were randomly divided into one of three groups: Group 1=isometric weight bearing exercise (vibration exercise), Group 2=exercise only and Group 3=vibration only. Initial baseline SBF was measured using a laser Doppler imager produced by MOOR Instruments, Inc (LDV 304, Oxford, England). Then, the subjects according to their assigned group performed isometric therapeutic exercise with or without whole body vibration or received vibration to their calf using Power Plate® vibration platform (Power Plate® North America, LLC, Culver City, California, USA). Skin blood flow was measured immediately after the intervention. The third measurement was taken after ten minutes of rest. The authors reported that the group that received vibration only showed significant increase in blood flow from baseline to post vibration (250%) and remained elevated at 10 minutes post intervention (200%) [(9)].

In the second study, the authors utilized two experiments to assess if a specific frequency or a specific duration of vibration was better in improving SBF. In first experiment, they selected 18 healthy subjects (mean age 20.3±2.9 years) and randomly placed them into 30Hz or 50Hz vibration group. In the second experiment, seven subjects (mean age 23.3±3.8 years) received 30 Hz vibration on one day and were asked to come the next day to receive 50 Hz. In both of these experiments, subjects received vibration to the underside of their forearm for 10 minutes using a vibration platform (Power Plate® North America, LLC, Culver City, California, USA). Subjects were instructed not to have eaten two hours prior to the vibration intervention. Skin blood flow was measured using laser Doppler flow meter (BioPac Systems, Golletta, CA) at baseline, during vibration and 15 minutes of recovery period.

Findings from the first experiment showed that SBF remained significantly elevated from fourth minute until the ninth minute in both 30Hz and 50Hz group. There was a significant decrease (90%, p=0.01) in SBF between the ninth minute to tenth minute of vibration. In addition to that, the fifth minute showed the highest percent increase in 50Hz (511%) vs. 30Hz (360%) groups. During the 15 minutes recovery period, SBF in the 30Hz group dropped below baseline (mean=78%) at the ninth minute and reached its lowest point (mean=74%) at the 15 minute recovery period. However, SBF in the 50Hz group did not return to the baseline (mean=128%) within the 15 minute recovery.

Results of the second experiment showed that significant increase was seen at the fourth minute in both 30Hz (293%) and 50Hz (513%) frequencies. Skin blood flow was higher throughout the vibration treatment and two minutes after. Skin blood flow in the

30Hz reached baseline (99%) at minute 5 of recovery, increased to 184% at minute 6. It continued to drop after ninth minute and reached to 65% of baseline at minute 15 of recovery. However, SBF in 50 Hz did not return to baseline (140%) and remained elevated during the 15th minute recovery period. Study findings from these two experiments suggested that passive vibration with a frequency of either 30 Hz or 50 Hz can significantly increase skin blood flow in the forearm within five minutes of passive vibration application. Based on the two experiments, the authors reported that passive vibration was quick and a feasible method to increase skin blood flow in a short period of time as opposed to the other methods that can lead to skin burns (hot packs), side effects (medications) or discomfort (exercise) [10].

In another study, ten type 2 diabetics with an average HbA1c level of 6.5% and ten age and body mass index (BMI) matched healthy adults, were tested. Subjects received vibration to their forearm using the Power Plate® (Power Plate® North America, LLC, Culver City, California, USA). Skin blood flow and blood concentrations of nitric oxide (NO) were measured at baseline, immediately after 5 minutes of vibration and 5 minutes after vibration was ceased. Skin blood flow was measured by using a laser Doppler meter (BioPac Systems, Golletta, CA). Results from this study showed that SBF was significantly increased in both healthy adults (461%) and type 2 diabetics (223%). Blood concentrations of NO was significantly higher in both the healthy group (374%) and the type 2 diabetics (258%) without any significant difference between the two groups [11].

In another study, ten healthy adult volunteers aged between 20-30 years participated, and received two interventions a day for 3 consecutive days: Intervention 1 -

active vibration only (vibration exercise), Intervention 2-passive vibration only, Intervention 3 - moist heat only, Intervention 4 – moist heat combined with passive vibration (MHPV), Intervention 5 – a commercial Sunbeam® Health at Home® massaging heating pad, and Intervention 6 - no intervention, rest. Power Plate® (Power Plate® North America, LLC. Culver City, California, USA) was used to deliver vibration. Skin blood flow and skin temperature was measured on the posterior aspect of the muscle belly of gastrocnemius at baseline, immediately after vibration and 10 minutes post vibration. Skin blood flow and skin temperature were measured using a laser Doppler flow meter produced by BioPac, Inc (BioPac Systems, Golletta, CA). The MHPV combination showed highest increase in SBF than in the passive vibration alone and moist heat alone groups from baseline to immediately after vibration. At the same time, increase in skin temperature was lowest in the MHPV combination group than in passive vibration alone and the moist heat alone groups. However, the passive vibration alone group showed significant increase in skin blood flow without significant increase in skin temperature as opposed to the moist heat alone group. These findings indicated that passive vibration can be a safe alternative method in increasing SBF in individuals at a greater risk of a burn [(12)].

In the follow up study, ten healthy elderly subjects between 55-73 years of age received two interventions for ten minutes each day for three consecutive days: Intervention 1- active vibration, Intervention 2- passive vibration, Intervention 3 – moist heat, Intervention 4 – moist heat combined with passive vibration (MHPV), Intervention 5 – a commercial Sunbeam® Health at Home® Massaging Heating Pad, and Intervention 6- rest. Passive vibration was delivered using the Physio Plate® (GLOBUS Physio Plate,

Domino S.R.L, San Vendemiano, Italy). Skin blood flow was measured using a laser Doppler imager (MOOR FLPI, V 2.1. Oxford, England). Skin temperature was measured using a thermistor (BioPac®, Inc, Goleta, California). Measurements were taken at baseline, immediately after vibration and 10 minutes post vibration. Results showed that the MHPV combination significantly increased SBF to 450% immediately after ten minutes of vibration and to 379% at 10 minutes post rest; more than any other interventions. A significant change in ST was found in the MHPV combination than the other interventions. Findings from this study showed that passive vibration can increase skin blood flow without increasing skin temperature in elderly individuals [13].

In another study, the authors examined the effect of PV with a frequency of 50 HZ in improving skin blood flow in type 2 diabetics. Eighteen subjects with type 2 diabetes mellitus between 47-74 years of age, and 18 age matched controls between 50-75 years of age received 10 minutes of PV. Passive vibration was delivered to the anterior aspect of their forearm and on the plantar aspect of the first three metatarsal heads using a vibration platform (GLOBUS Physio Plate, Domino S.R.L, San Vendemiano, Italy). Skin blood flow was measured at baseline, post vibration and 10 minutes post rest using a laser Doppler imager (MOOR FLPI, V 2.1. Oxford, England). Findings showed that there was a significant difference in the foot and forearm SBF across time for both groups. Diabetics showed the greatest percent increase in the foot SBF (118.5%) from baseline to end of vibration vs. non diabetics (37.62%). However, there was no significant change in mean SBF in forearm vs. foot across time between groups. Study findings suggested that passive vibration can increase SBF in type 2 diabetics [14].

Conclusion

Overall, the study findings from the Department of Physical Therapy, LLU suggest that: 1) Passive vibration is a safe method as opposed to other methods such as hot packs, medications and exercise in increasing skin blood flow in the individuals who are at a greater risk of burns, 2) Passive vibration can increase skin blood flow in healthy younger adults, healthy elderly and type 2 diabetics, 3) Passive vibration can significantly increase SBF in the forearm and foot with the subjects in the sitting position and in the calf area with the subjects in the lying position, 4) Significant increase in SBF can be obtained within five minutes of vibration, 5) SBF can remain elevated for at least nine minutes during the vibration application, 6) SBF remains elevated for at least seven minutes following the vibration application, and 7) The combination of moist heat and passive vibration can significantly increase SBF in the calf area without significantly increasing skin temperature.

Several lines of evidence suggest that clinicians can use passive vibration to improve skin microcirculation [(6), (9), (10), (11), (12), (13), (14)]. This may reduce ulcer and other skin complications that are associated with aging and diabetes. Clinical trials are needed to determine the possibility of reducing diabetic ulcer as a result of passive vibration.

References

1. Sales PM, Souza PM, Simeoni LA, Silveira D. alpha-Amylase inhibitors: a review of raw material and isolated compounds from plant source. J Pharm Pharm Sci. 2012;15(1):141-83.

2. National Diabetes Clearinghouse. (January 22, 2013). Insulin Resistance and Prediabetes. Retrieved March 22, 2013 from http://diabetes.niddk.nih.gov/dm/pubs/insulinresistance/index.aspx.

3. McLellan K, Petrofsky JS, Zimmerman G, Lohman E, Prowse M, Schwab E, et al. The influence of environmental temperature on the response of the skin to local pressure: the impact of aging and diabetes. Diabetes Technol Ther. 2009 Dec;11(12):791-8.

4. Petrofsky JS. Resting blood flow in the skin: does it exist, and what is the influence of temperature, aging, and diabetes? J Diabetes Sci Technol. 2012 May;6(3):674-85.

5. Charkoudian N. Skin blood flow in adult human thermoregulation: how it works, when it does not, and why. Mayo Clin Proc. 2003 May;78(5):603-12.

6. Wiernsperger NF, Bouskela E. Microcirculation in insulin resistance and diabetes: more than just a complication. Diabetes Metab. 2003 Sep;29(4 Pt 2):6S77-87.

7. Watkins PJ. The diabetic foot. BMJ. 2003 May 3;326(7396):977-9.

8. Mester J, Kleinoder H, Yue Z. Vibration training: benefits and risks. J Biomech. 2006;39(6):1056-65.

9. Lohman EB, 3rd, Petrofsky JS, Maloney-Hinds C, Betts-Schwab H, Thorpe D. The effect of whole body vibration on lower extremity skin blood flow in normal subjects. Med Sci Monit. 2007 Feb;13(2):CR71-6.

10. Maloney-Hinds C, Petrofsky JS, Zimmerman G. The effect of 30 Hz vs. 50 Hz passive vibration and duration of vibration on skin blood flow in the arm. Med Sci Monit. 2008 Mar;14(3):CR112-6.

11. Maloney-Hinds C, Petrofsky JS, Zimmerman G, Hessinger DA. The role of nitric oxide in skin blood flow increases due to vibration in healthy adults and adults with type 2 diabetes. Diabetes Technol Ther. 2009 Jan;11(1):39-43.

12. Lohman EB, 3rd, Bains GS, Lohman T, DeLeon M, Petrofsky JS. A comparison of the effect of a variety of thermal and vibratory modalities on skin temperature and blood flow in healthy volunteers. Med Sci Monit. 2011 Sep;17(9):MT72-81.

13. Lohman EB, Sackiriyas KSB, Bains G, Calandra G, Lobo C, Nakhro D, et al. A comparison of whole body vibration and moist heat on lower extremity skin temperature and skin blood flow in healthy older individuals. Med Sci Monit. 2012;18(7):CR415-24.

14. Lohman EB, Sackiriyas KS, Bains G, Dhamane KH, Solani KJ, Raju C, K., et al. Effect of Vibration on Skin Blood Flow in Type 2 Diabetes Mellitus (accepted). ijpot. 2013.

APPENDIX A

INFORMED CONSENT

LOMA LINDA UNIVERSITY

School of Allied Health Professions

Informed Consent

"The effect of vibration on skin blood flow, skin temperature, and blood pressure in good controlled versus poor controlled type 2 diabetes mellitus"

Purpose and Procedures

You are invited to participate in a research study that will analyze lower leg skin blood flow following vibration of good controlled versus poor controlled type 2 diabetics between 18 to 75 years of age. Decreased blood circulation is associated with diabetes mellitus and can lead to decreased skin healing, ulcerations and amputation. The purpose of this study is to determine if the application of vibration improves skin blood flow in both good controlled and poor controlled diabetics. The effect of vibration on good controlled type 2 diabetics is compared with the age and gender matched poor controlled type 2 diabetics in order to measure the differences between these two groups.

Upon arrival you will be led into a room where room temperature will be set at 71.6° F-75.2° F and between 35% and 40% humidity. Your age, weight, height, race, and activity level will be recorded. You will be asked to submit a copy of your hemoglobin A1c report or it may be collected from Diabetic Treatment Centre, Loma Linda University. You will be rested for 30 minutes and be given a short questionnaire to help determine the appropriateness of your participation in this study. Next, to rule out a possible blood clot in your lower leg, you will be asked to lie on your back and your ankles will be flexed to end range with your knees straight. You will be asked to report any pain or discomfort. The girth of your calf muscle will be measured and your legs will be felt for tenderness and warmth and a visual inspection of your lower legs will be administered. The underside of your calf and the bottom of the foot near the great toe will be marked with a safe-skin ink to ensure that blood flow (non-invasive Laser Doppler scans), skin temperature (BioPac systems), and blood pressure readings will be measured in the same location for both pre and post test recordings. Baseline readings will then be recorded with sensors placed at 90° angle to your calf and foot. You will then receive vibration to your calf for 10 minutes and foot for 10 minutes. Once the vibration stops, readings will be recorded immediately. A third recording will be taken after 10 minutes following vibration.

All testing will take place in Nichol Hall, Room A-620. The whole procedure will take approximately 2 hours.

Subject's initials _____ Date _____

A Seventh-day Adventist Institution
DEPARTMENT OF PHYSICAL THERAPY | Nichol Hall, Loma Linda, California 92350
(909) 558-4632 · (800) 422-4558 · fax (909) 558-0459 · www.llu.edu/llu/sahp/pt

"The effect of vibration on skin blood flow, skin temperature, and blood pressure in good controlled versus poor controlled type 2 diabetes mellitus"

Risks

Participation in this study involves some risks, no greater than day-to-day life. There may be temporary redness and itchiness on the application site as a result of the vibration.

Benefits

There is no direct benefit to you for participating in this study. However, this study will provide future researchers with information regarding vibration and skin blood flow in diabetics.

Participant's rights

Participation is completely voluntary. You may leave the study at any time without penalty.

Confidentiality

Subjects will be provided with an identification number (ID) and the file will be locked in a cabinet. All records will be confidential. We will not disclose your participation without your written permission. Any published document resulting from this study will not disclose your identity.

Costs/Compensation

There is no cost for participating in this study. The subject will receive a $25 gift card for participating.

Impartial Third party

If you wish to contact a third party not associated with the study for any questions or a complaint, you may contact the Office of Patient Relations at Loma Linda University, Loma Linda University Medical Center, Loma Linda California 92354. Phone (909) 558-4647.

Subject's initials _____

Date _____

"The effect of vibration on skin blood flow, skin temperature, and blood pressure in good controlled versus poor controlled Type 2 diabetes mellitus"

Informed consent statement

I have read the contents of the consent form and have listened to the verbal explanation given by the investigator. My questions regarding the study have been answered to my satisfaction. This study has been explained to me at a level that I can comprehend and I give my consent to participate in the study. Signing this consent document does not waive my rights nor does it release the investigators, institutions, or sponsors from their responsibilities. I may call Everett B. Lohman III, DSc, PT, OCS, principle investigator, during regular office hours at (909) 558-1000, extension 83171 if I have additional questions or concerns. During non-office hours a voice mail message can be left at this number.

I have received a copy of this consent form.

_____ _____

Signature of Subject Date

Investigator's Statement

I have reviewed the consent form with the person signing above. I have explained potential risks and benefits of the study.

Signature of Investigator _____ Date _____

APPENDIX B

DEMOGRAPHIC DATA

Demographic Data				
Informed Consent:	Yes	No	(Circle Correct Response)	
Subject Identification Number:				
Age:	Gender:	Height:	Weight:	
Physical Activity:	Very Light/ Light/ Moderate/ Heavy/ Exceptional			
Ethnicity: American Indian or Alaska Native/ Asian/ Black or African American/ Hispanic or Latino/ Native Hawaiian or Other Pacific Islander/ White/ Other:				

Exclusion		Comments
Circulatory disorders	Yes ( )	No ( )
Deep vein thrombophlebitis or other bleeding disorders	Yes ( )	No ( )
Pregnant	Yes ( )	No ( )
Is it possible that you may be pregnant	Yes ( )	No ( )
Pacemakers	Yes ( )	No ( )
Cancer	Yes ( )	No ( )
History of Heart Disease	Yes ( )	No ( )
Skin Ulcers	Yes ( )	No ( )
Neurological or Orthopaedic Disorders	Yes ( )	No ( )

Homan's Sign Test	+	-
Assess for pain, pallor, swelling, tenderness or warmth to palpation:	Yes	No
Calf muscle girth	Right:_____ in/cm	Left: _____in/cm

Well's Clinical Prediction Rule for Deep Vein Thrombosis	Score
Active cancer?	Yes (1 Points)
Bedridden recently 3 days or major surgery within four weeks?	Yes (1 Points)
Calf swelling 3 cm compared to the other leg	Yes (1 Points)
Collateral (non-varicose) superficial veins present?	Yes (1 Points)
Entire leg swollen?	Yes (1 Points)
Localized tenderness along the deep venous system?	Yes (1 Points)
Pitting edema, greater in the symptomatic leg?	Yes (1 Points)
Paralysis, paresis, or recent plaster immobilization of the lower extremity	Yes (1 Points)
Previously documented DVT?	Yes (1 Points)
Alternative diagnosis to DVT as likely or more likely	Yes (-2 Points)
A score of ≥2 will be excluded from the study.	Total Score: _____

Semmes-Weinstein Test®: At test site location					(Circle one response)
2.83	3.61	4.31	4.56	5.07	6.65

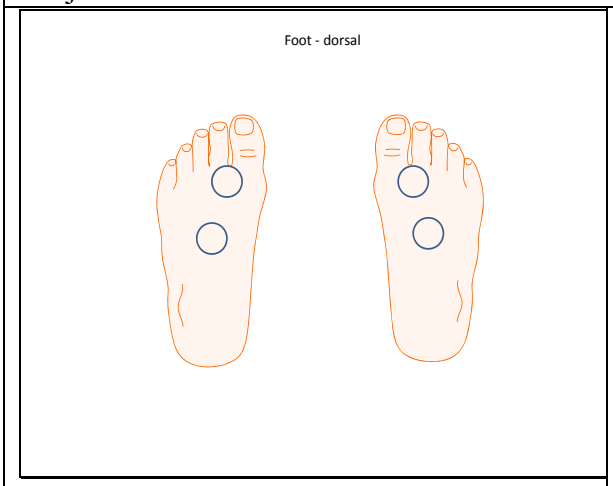
A1c Level:		
Decision :	□ Include in the study	□ Exclude in the study

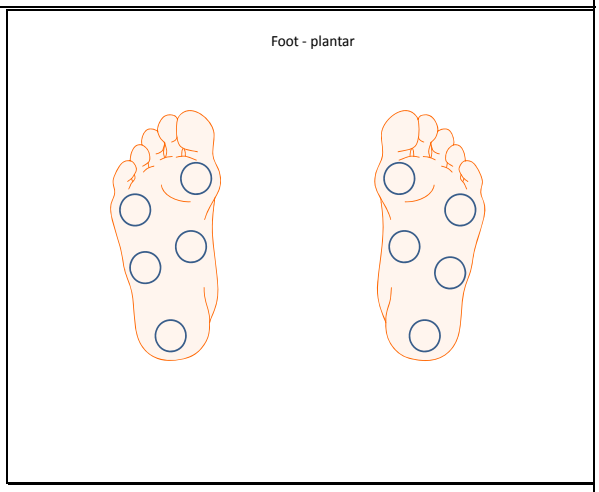
APPENDIX C

FOOT MAPPING FORM

Semms-Weinstein Monofilament – Sensory Foot Mapping

Subject Number:





Evaluator size	Target Force (g)	Representation	Dorsal Thresholds	PlantarThresholds
2.83	0.07	Green	Normal	Normal
3.61	0.4	Blue	Diminished light touch	Normal
4.31	2.0	Purple	Diminished protective	Diminished light touch
4.56	4.0	Red	Loss of protective	Diminished protective
5.07	10.0	Red	Loss of protective	Loss of protective
6.65	300.0	Red	Deep pressure only	Deep pressure only

Impressions: