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The Effects of Axial Bone Osteogenic Loading-Type Resistance Exercise on Adults with Risk of Moderate-Metabolic Dysfunction: A Pilot Study

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Abstract

Objective: To determine the efficacy of osteogenic loading (OL) on glycemic control in older adults with pre-type 2 diabetes.

Research design and methods: We performed a 24-week observational trial in 21 adults (10 females and 11 males; mean age 62 (+/- 11.8 SD) years) with pre-type 2 diabetes. Subjects were randomly asked by their general practitioner (GP) to participate in supervised OL therapy, which had previously been used to treat bone mass loss [1] but had anecdotally suggested to have positive implications on patients who also had metabolic dysfunction [2]. Metabolic syndrome abnormalities, mean glycated hemoglobin (HbA1c) levels, and mental wellbeing markers were determined before and after the intervention.

Results: Twenty-four weeks of OL therapy (sessions one time per week) resulted in significantly reduced mean HbA1c levels from 6.37 (+/- 1.11 SD) to 5.81 (+/- 1.01 SD) (P<0.05). No significant weight or BMI change occurred and no adverse events or complications occurred with any of the test subjects.

Conclusions: OL therapy as a supplement to standard care is both feasible and effective in improving glycemic control among moderate-risk adults with poor glycemic control. Significant reductions were measured in HbA1c levels amongst group subjects by 8.8% (+/- 4.1% SD) from baseline to post-test without weight or BMI change.

Introduction

According to the World Health Organization (WHO), type 2 diabetes patients worldwide total 347 million, accounted for 1.5 million deaths in 2012, and by 2030 will represent the seventh leading cause of death around the world. [3-5]. Amongst South and East Asian, and Afro-Caribbean populations, diabetes prevalence is double that of Caucasians [6]. This is a concern given the general disparate access and substandard health care among minorities [7]. Physical medicine interventions (e.g. exercise and physiotherapy) have seen success with the type 2 and pre-type 2 populations.

Aerobic exercise has consistently been shown to improve glucose control [8-10] and improve insulin sensitivity [11,12]. Congruent with this evidence, the American Diabetes Association (ADA), as well as the NICE guidelines recommend that individuals with type 2 diabetes perform a minimum of 150 minutes of moderate-intensity aerobic exercise and/or at least 90 minutes of vigorous aerobic exercise per week [13,14]. Even though such a minor lifestyle modification could have a substantial impact on the metabolic health of this population, it is often difficult for those who have a sedentary lifestyle to adhere to these guidelines. A recent population-based study found that only 28% of individuals with type 2 diabetes achieve these recommendations [15]. Unfortunately, it is frequently those who would benefit the most from aerobic exercise that have the greatest difficulty engaging in it. For individuals with severe obesity, arthritis, physical disabilities, and/or diabetes complications, even walking for 20–30 minutes may be difficult, uncomfortable, or even painful, thereby making it impractical to expect wide adherence. With the prevalence of type 2 diabetes [16] continually increasing worldwide, it is evident that alternate forms of physical activity that produce similar metabolic improvements to aerobic exercise may be beneficial in the management of this disease.

More recently, resistance exercise has been recognized as a useful therapeutic tool for the direct treatment of a number of chronic diseases [17-21]. Obese [22] and elderly [23,24] populations have consistently been seen garnering the benefits of resistance exercise safely. Resistance exercise has also been found to improve insulin sensitivity and glycemic control [25-27]. Though the ADA [28] and the American College of Sports Medicine [29] recommend the use of resistance exercise as part of treatment protocols for diabetic patients, basic exercise and safety techniques are often required, making the accessibility for resistance type of exercise protocol challenging without initial instruction. Adherence to resistance exercise therapy could potentially increase with more targeted protocols and a specialized exercise apparatus conducive to those suffering the effects of diabetes. In prior analysis of structured aerobic exercise programs (including: walking, cycling, and resistance exercise), absolute reductions of blood glucose levels have been seen by approximately 0.66% [30,31].

We seek to apply higher forces than are typically used in resistance exercise by using an axial bone loading apparatus that is typically used for osteoporosis treatment (OL) [1]. This could potentially stimulate a similar density adaptation in muscle tissue increasing insulin receptor sites, and thereby blood glucose management as seen in resistance exercise meta-analysis literature [32,33]. The exercise protocol with this apparatus is more infrequent and shorter in duration per session than

any exercise recommendation the ADA is currently making. Previously, OL use with osteoporosis patients has shown greater compliance than with most physical medicine or exercise recommendations [2].

Methods

Design

We conducted a 24-week, single-center, randomized, observational trial with a pre-type 2 diabetes population. A single group of 11 male subjects and 10 female subjects (N=21) were selected at random by their GP and referred to the OL therapy program. Subjects were to complete the once per week therapy intervention with a minimum of 18 sessions completed at the conclusion of the 24 weeks without dietary modification. A small sample size was chosen in order to determine if a larger study is required. The study was approved by the Chief Clinical Director and the independent review board of the First 4 Health Group (part of the United Kingdom National Health Services (NHS)).

Setting

The OL therapy intervention took place at a single NHS facility located, Stratford Village Surgery (SVS), in the London Borough of Newham, England. Registered Health Psychologist at the SVS supervised the intervention. NHS technical staff at SVS supervised intervention.

Participants

Subjects between the ages of 40 and 92 were referred at random to participate in this study by their GP. The wide variance in age was used so that observations can be made on exercise/OL therapy response can be ascertained from younger to older, and viewed in a case by case basis. Individual outcomes are posted for this reason. One out of every 3 was asked if they wanted to participate in this study through their regular appointments. Patient invitations were continually given until the study population was full, and patients were seen in no particular order, therefore subject selection was random. The mean age by participants was 62. By reading fasting HbA1c of 5.1 or higher, the inclusion criteria allowed for subjects with increased risk of metabolic dysfunction.

Interested subjects were excluded if: 1) limitations or contraindications to ambulatory and/or resistance training exercise are present (assessed via the required NHS exercise referral screening form); 2) acute illness or injury is present; 3) exercise or physical activity restrictions have been imposed by their health care provider; 4) female participants are of childbearing age/potential *and* pregnant *or* trying to become pregnant within 1-year from their recruitment date; 5) there is a history of or current problems with syncope (loss of consciousness or fainting); 6) elevated blood pressure ($\geq$ 140 mmHg systolic or $\geq$ 90 mmHg diastolic) measured at their baseline testing session and is not actively being controlled by medication while under the supervision of licensed health care provider; 7) the participant has experienced a stroke (hemorrhagic or thrombotic) within the past 12-months; 8) the participant has been treated for or has a history of an aneurysm (ballooning of a blood vessel); 9) the participant is undergoing current insulin therapy; 10) the participant is engaging in exercise or exercise type activity, 2 or more times weekly for 20 minutes or longer per session or in any resistance training during the previous 6 months; 11) the participant had changes during the previous 2 months in oral hypoglycemic, antihypertensive, or lipid-lowering agents; or 12) the participant experienced more than a 5% reduction in body weight over the past 2 months. Subjects would also be excluded from the final analysis if they attended less than required 18 of the 24 weekly sessions.

Randomization and blinding

After patients were referred at random by their GP, they contacted the principal investigator and were informed about the study. They were then screened for aforementioned exclusion criteria to become a subject. As there was no control group, and this was an observational study, the subjects could not be blinded. However, the blood analysis was conducted by NHS staff, none of whom knew which of the patients in the clinic were subjects in the study, therefore, the blood analysis portion was blinded. The blood analysis was performed by SVS lab technicians.

Intervention

The initial test group (N=21) was asked to return to the SVS one time per week at a regularly scheduled interval to complete one OL session. There was no variation in duration or intensity of the OL protocol from the baseline session to subsequent sessions. Subjects were told to engage to their perceived maximum force/loading level while not reaching a point of discomfort. The protocol included: one compressive movement with upper extremities; one movement with lower extremities; one movement with core activation; and one movement with spinal compressive forces recruited, for a total of 4 movements with a total exercise time of 15 minutes. Though the 4 movements each last only 5 seconds in duration, the device adjustments are specific (to the mm), and take the full 15 minutes to identify the correct optimal axial compressive positions. The same protocol is used for bone density treatment with the emphasis being placed on maximum muscular recruitment in positions of optimal leverage and biomechanics for the greatest-self-controlled axial loading of bone [1,2,34,35]. The force/loading levels were tracked in each movement and for each session via Internet cloud tracking software to ensure no loss of data. Subjects were instructed not to change their eating habits during the intervention.

Outcomes and measurements

The primary outcome was the absolute difference in value between baseline blood glucose levels and post 24-week intervention blood glucose levels. Secondary outcomes reported were changes or lack of changes in bodyweight as well as psychological measures. Mental wellbeing of subjects was evaluated, and they were informed that values of mental well-being would be collected pre-mid-and post-study to see if outlook on their health had changed with this intervention. NHS lab Technicians took recorded both pre-and post-fasting blood glucose levels in all subjects who were blended into their regular patient load, thereby blinding Technicians to which individuals were subjects in this study. Blood analysis was done with the Variant 11 machine, Bio-Rad UK distributors, Bio-Rad House, Maxted Road, Hemel Hempstead Herts, HP2 4PD. OL therapy was performed with bioDensity™, manufactured by Performance Health Systems LLC., 401 Huehl Road, Suite 2a, Northbrook, IL. United States.

Technicians also measured bodyweight at the baseline OL appointment, as well as at the conclusion of the 24 weeks. The measurement schedule was as follows:

Each time a subject arrived for the OL session, standard procedure was to inquire if subjects have had any physical problems, issues, pain, discomfort, or other issues since their last OL session. Typically, subjects would call, e-mail, or volunteer this information before their next session without being prompted. However, we include this procedure to help maximize safety for participants by screening for complications, contraindications, or adverse events, related or not to their previous OL sessions.

Adverse events and compliance

There were no adverse events during the 24-week intervention, however 4 of the male subjects did not achieve the minimum 18 OL sessions required and were therefore removed from the final analysis. In all four of the lack of compliance cases, poor attendance did not result from factors (e.g. injury) inside of the study.

Statistical analysis

We tested if there were differences between pre-post-fasting blood glucose measures, which could give reason for a larger double-blinded study. Pre-post measures were analyzed as a T-test of dependent variables and the hypothesis was that there would be a difference/reduction between the pre-post HbA1c measures.

Results

The pre-post measures resulted in reduced mean HbA1c levels from 6.37 (+/- 1.11 SD) to 5.81 (+/- 1.01 SD). These data represents a mean absolute blood glucose reduction by 8.8% (+/- 4.1% SD) over the 24-week intervention, and a significant reduction was seen comparing the pre-post HbA1c measures (P<0.05). No significant changes in weight or BMI occurred.

The secondary pre-post psychological measures resulted in increase mean wellbeing measures from 50 (+/-13.4 SD) to 58 (+/-9.12 SD). Thus, representing a mean positive change in mental wellbeing of subjects by 8 points over the 24-week intervention (Tables 1 and 2).

Discussion

We saw a statistically significant reduction in the HbA1c measures of subjects with the 24 weeks/sessions of OL. It is important to point out that the significant changes in blood glucose management occurred without significant body weight changes, or changes in BMI. This can indicate change in density of muscle cells from a myofibril standpoint, resulting in greater ability for insulin reception. We chose a low risk population for this test because we wanted to control dietary intake and food choices while ensuring that there was no significant weight or BMI change. It would not be appropriate to ask a higher-risk diabetic population to not change their diet, which is in effect asking them to continue to consume the same or similar unhealthy diet for the purposes of a study.

The OL type of therapy that was employed in this study shows a level of force/loading and exercise intensity (work done vs. time under load) greater than most seen in academic literature. This analysis showed individuals producing peak forces of 7.75 (+/- 2.21 SD) MOB of loading in the lower extremities, 3.13 (+/- 0.98 SD) MOB in the upper extremities, and 1.9 (+/- 0.42 SD) MOB of loading in the spine. Since previous literature has shown that higher intensity muscular engagement type exercise had potentially greater effect on glycemic control [25-27], we hypothesized that OL therapy may show an advanced effect, as the exercise intensity experience was greater than previously tested. This study indicates the positive implication to confirming hypothesis, as well as showing some ability to increase patient compliance with more targeted therapies. The mechanism of increased glycemic control with

Subject	Age	Ethnicity	Gender	Ht cm	Pre-Weight Kg	Post-Weight Kg	Pre-HbA1c	Post-HbA1c	Abs Reduc	% Reduc	Comp OL Sessions
1	42	African	M	176	116	114	6.60	5.90	0.70	10.6%	24
2	84	Pakistani	M	173	82	82	7.50	7.20	0.30	4.0%	24
3	60	British	M	178	85	84	6.60	6.00	0.60	9.1%	24
4	52	Bangladeshi	M	181	83	84	5.80	5.90	-0.10	-1.7%	23
5	64	Indian	M	175	73	70	5.80	5.30	0.50	8.6%	24
6	58	Indian	M	169	80	78	8.60	7.80	0.80	9.3%	24
7	78	British Indian	M	174	66	66	5.50	5.40	0.10	1.8%	24
8	92	Indian	M	156	62	60	5.10	4.60	0.50	9.8%	21
9	63	Indian	M	170	82	77	6.90	5.90	1.00	14.5%	24
10	52	Caribbean	F	170	65	63	5.10	4.60	0.50	9.8%	20
11	63	Filipino	F	154	56	55	5.50	4.80	0.70	12.7%	24
12	60	Indian	F	147	55	55	5.30	4.60	0.70	13.2%	24
13	53	African	F	163	79	78	6.60	5.90	0.70	10.6%	21
14	67	British Indian	F	147	62	59	6.10	5.60	0.50	8.2%	24
15	40	African	F	171	112	110	6.30	5.70	0.60	9.5%	18
16	59	White British	F	159	85	84	6.10	5.60	0.50	8.2%	24
17	63	Filipino	F	154	74	76	8.90	7.90	1.00	11.2%	23
18	59	Indian	M	178	76	N/A	5.60	DROP	N/A		7
19	57	Indian	M	175	112	N/A	6.70	DROP	N/A		11
20	65	African	M	175	110	N/A	7.00	DROP	N/A		11
21	56	British Pakistani	M	165	72	N/A	6.30	DROP	N/A		9
Mean	**62**				**77**	**76**	**6.37**	**5.81**	**0.57**	**8.8%**	
SD	**12.1**				**17.0**	**16.9**	**1.11**	**1.01**		**4.1%**	

Table 1: Baseline measures, forms and physiological profile, bodyweight, mid-intervention measures and physiological profile, and post- intervention measures, bodyweight, and physiological profile.

Subject	Age	Ethnicity	Gender	Ht cm	% Force Prod Incr	Peak UE MOB Loading	Peak LE MOB Loading	Peak Spine MOB Loading	Peak UE Force/ Loading KG	Peak LE Force/ Loading KG	Peak Spine Force/ Loading KG
1	42	African	M	176	111	3.32	7.59	1.44	385	880	167
2	84	Pakistani	M	173	77	1.82	4.12	1.26	149	338	103
3	60	British	M	178	114	4.08	11.14	2.45	347	947	208
4	52	Bangladeshi	M	181	136	3.78	9.66	2.16	314	802	179
5	64	Indian	M	175	77	4.90	10.00	2.36	358	730	172
6	58	Indian	M	169	92	2.01	3.09	1.30	161	247	104
7	78	British Indian	M	174	134	4.30	7.11	2.30	284	469	152
8	92	Indian	M	156	136	2.77	5.50	1.90	172	341	118
9	63	Indian	M	170	114	4.91	9.32	1.98	403	764	162
10	52	Caribbean	F	170	70	3.11	8.69	2.02	202	565	131
11	63	Filipino	F	154	101	2.98	8.25	2.32	167	462	130
12	60	Indian	F	147	115	2.47	8.25	2.29	136	454	126
13	53	African	F	163	130	3.27	10.14	1.92	258	801	152
14	67	British Indian	F	147	87	1.90	6.13	1.92	118	380	119
15	40	African	F	171	70	2.48	6.79	1.12	278	761	125
16	59	White British	F	159	136	2.48	9.47	1.52	211	805	129
17	63	Filipino	F	154	182	2.57	6.57	1.99	190	486	147
18	59	Indian	M	178	DROP						
19	57	Indian	M	175	DROP						
20	65	African	M	175	DROP						
21	56	British Pakistani	M	165	DROP						
Mean	**62**				**110.7**	**3.13**	**7.75**	**1.90**			
SD	**12.1**				**29.3**	**0.98**	**2.21**	**0.42**			

Table 2: Measures for force/loading created in each movement as well as changes in force produced were also tracked and reflected as loading in multiples of bodyweight (MOB) in.

this intervention may relate to GLUT4 signaling. GLUT4 density has been shown to increase by 40% with high intensity resistance training [36]. Resistance exercise that is associated with fatigue of the structure of the muscle cell, as opposed to fatigue associated with ATP stores, has a myofibril protein syntheses (MPS) implication [37]. OL allows for fatigue of a muscle (or muscle group) in this structural fashion and based on the MOB loading levels seen here, possibly stimulating more MPS that the majority of other activities seen in therapy or exercise. This MPS adaptation thereby requires more glucose processed into the muscle cells via the GLUT4 signaling to meet with this MPS demand. More research is required using OL type therapy with metabolic syndrome patients and effects on glycemic management.

Mental wellbeing relates to a person's psychological functioning, life-satisfaction and ability to develop and maintain mutually benefiting relationships [38,39]. In this study, secondary outcome mental wellbeing measures of subjects were evaluated, to see if there would be a change in psychological wellbeing as a result of the intervention. The analysis showed a positive change in mental wellbeing in all subjects. However, ongoing research is still required to assess the extent to which it is appropriate to use the Warwick-Edinburgh Mental Well-being Scale (WEMWBS) to assess mental well-being among different ethnic minority populations in the UK and the rest of the world.

Financial Conflicts of Interest

Second author has ownership/financial interest in Performance Health Systems, LLC., a corporation that manufactures and distributes the OL apparatus used in this analysis. The second author participated in the study for protocol education of the research team, and accurate intervention description in drafting of this manuscript. Primary author, and principal investigator has no financial interest.

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