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Is weight loss an effective treatment of pain symptoms related to knee joint osteoarthritis in obese adults?

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A SELECTIVE EVIDENCE BASED MEDICINE REVIEW

In Partial Fulfillment of the Requirements For

The Degree of Master of Science

In

Health Sciences – Physician Assistant

Department of Physician Assistant Studies
Philadelphia College of Osteopathic Medicine
Philadelphia, Pennsylvania

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Abstract

Objective: The objective of this selective EBM review is to determine whether or not weight loss is an effective treatment of pain symptoms related to knee joint osteoarthritis in obese adults.

Study Design: Systematic review of 2 randomized-controlled trials and 1 cohort study. All three articles were published in English between 2011-2015.

Data Sources: Two randomized, un-blinded, controlled studies and one cohort found using Pubmed.

Outcomes Measured: Each study evaluated change in pain symptoms related to knee osteoarthritis in obese adults as compared to weight loss.

Results: Studies showed that weight loss lead to a decrease in osteoarthritis knee pain.

Conclusions: These studied showed that weight loss in obese adults is an effective treatment for knee pain due to osteoarthritis. All studies showed a decrease in pain symptoms with weight reduction, regardless of the type of weight loss intervention.

Key Words: Osteoarthritis, obesity, pain, and weight loss

Introduction

Osteoarthritis (OA) is a degenerative joint disease characterized by narrowed joint space, osteophyte formation, increased density of subchondral bone, and bony cysts. The most commonly affected joints include cervical and lumbosacral spine, hip, knee, and first metatarsal phalangeal joint (MTP).¹ OA occurs when the anatomical joint protectors fail. These protectors include the joint capsule, ligaments, tendons, muscle, sensory afferents, synovial fluid, and cartilage. The joint capsule, ligaments, and tendons create a fixed range of motion for the joint, preventing dislocation and injury. Muscles and tendons also meticulously control muscle contraction, thereby decreasing joint load on impact and distributing impact evenly throughout the joint space. Mechanoreceptor sensory afferent nerves are found in the overlying skin, ligaments, and tendons. As the joint moves, these mechanoreceptors fire at different frequencies, through the spinal cord to muscles and tendons. This communication allows the muscles and tendons to accommodate for movements and provide optimal protection depending on the joint motion and impact. Synovial fluid provides lubrication for the articular cartilage surfaces, decreasing damage due to friction wear. Hyaluronic acid and lubricin are produced by synovial fibroblasts, and are crucial for production of the synovial fluid. Synovial fibroblast concentration is greatly decreased by inflammation as a result of joint injury.¹ Cartilage covers the bone ends of every joint, providing a thin layer of lubricated tissue to absorb impact and protect the bones. Any defect of these joint protectors increase the risks for development in OA, for example, muscle weakness, loss of sensation, traumatic injury to surrounding knee joint structures, and increased load on the joint due to obesity. This paper evaluates two randomized controlled trials and one cohort study, introducing weight loss plans, and comparing patient's pain symptoms in relation to amount of weight loss.

Age is the greatest risk factor for the development of OA.¹ With our aging population and increasing lifespans, arthritis management is becoming more prevalent in primary care settings. Knee joint arthritis (KJA) is seen in 37.4 % of patients over the age of 60 have.² In 2011, there were 757,000 total knee replacements performed, with osteoarthritis accounting for 95%. And in 2009 alone, \$28.5 billion was spent on hospital expenditures related to total knee joint replacements. It is estimated that 44 million primary care visits each year are for arthritis.²

Modifiable risk factors for knee OA include weight, injury/trauma, occupation and overuse, muscle weakness, misalignment, and joint laxity. While walking, 3-6 times a person's body weight is transmitted through the knee joint.¹ So for every one pound gained, there is an increase of three to six pounds on the joint. Non-modifiable risk factors include age, race, gender, and genetic predisposition. Arthritis is generally more common in females than males, and less commonly seen in Asians. OA is a clinical diagnosis based on symptoms and physical exam, but standing radiographic studies are used to confirm the diagnosis. The criteria for diagnosing knee OA is knee pain, plus three or more of the following characteristics; Age > 50, crepitus, morning stiffness lasting less than 30 minutes, tenderness of the knee, bony enlargement of the knee, and no increased warmth of the knee to touch.

The manifestations of OA pain symptoms are not well known. Cartilage is aneural, so the pain is thought to be generated from innervated structures surrounding the cartilage, such as synovium, joint capsule, muscles, ligaments, and subchondral bone. Although there is extensive research in the topic, currently there are no readily available procedures on the market to repair or regenerate already damaged knee joint cartilage. Thus, prevention and management are the two major keys in treatment of OA.

Usual methods of treatment for KJA include weight loss, physical therapy, acetaminophen, NSAIDs, corticosteroid and hyaluronic acid injections, and total knee replacements. A total knee replacement is the most definitive treatment but also the most invasive. All other treatment options listed above are modalities to manage the symptoms related to OA.

As discussed above, knee joint OA is a huge health care expense, with \$28.5 billion spent on hospital expenditures related to total knee joint replacements in 2009. This dollar amount does not include the cost of outpatient visits, OTC medications, prescriptions NSAIDs, physical therapy, and injection procedures. Weight loss is an understated treatment option that can be pursued with little or no expense to help symptoms related to knee joint OA. By providing information and encouraging weight loss in patients with OA, healthcare providers can better manage patient symptoms and decrease healthcare expenditures.

Objectives

The objective of this selective EBM review is to determine whether or not weight loss an effective treatment of pain symptoms related to knee joint osteoarthritis in obese adults.

Methods

This research study evaluated two RTCs and one cohort study. To participate in the research studies, participants were required to be at least 18 years of age, have a diagnosis of knee joint OA, have a BMI ≥ 29 kg/m², knee pain, and desire to lose weight. In the two RCTs weight loss interventions were implemented. The first RCT by Bliddal split the participants into

two groups. One group received 810 kcal/day for eight weeks, followed by 1200 kcal/day for 24 weeks, then 810 kcal/day for the last eight weeks. The second group was instructed on a 1200 kcal/day diet for all 26 weeks.³ In the second RCT by Christensen, all the participants engaged in a 16-week intense dietary program and then were randomized into three different groups. The first group continued with an intense diet plan, the second group was given an exercise regimen, and the third group was given no instruction at all.⁴ The cohort study by Riddle contained no interventions, only observation. At the end of the cohort, participants were evaluated based on their change in weight. The main outcomes evaluated in this study were decreased in pain symptoms as compared to weight loss.⁵

The author searched articles using PubMed. Key words in the search included osteoarthritis, obesity, pain, and weight loss. Articles were considered if they were written in English, published in peer-reviewed journals within the past 15 years and relevant to the clinical question. Types of articles included RCTs, cohorts, and studies that were POEM oriented. The studies evaluated and reported numbers needed to treat (NNT), absolute risk reduction (ARR), confidence intervals (CI) and *p*-values. Table 1 below shows the demographics and characteristics of each study as well as exclusion and inclusion criteria.

Table 1: Demographics and characteristics of included studies

Study	Type	# of pts	Age	Inclusion criteria	Exclusion criteria	W/d	Intervention
Bliddal H,2011	RCT	89	36-90, mean age = 63	Over 18 with primary knee OA diagnosed according to American College of Rheumatology criteria,	History of other rheumatic diseases, DM, or substantial abnormalities in hematologic, hepatic, renal, or cardiac	33	-Very low energy diet of 810 kcal/day x 8 weeks, 1200 kcal/day x 24 weeks, then 810 kcal/day x 8 weeks -Control group: Nutritional advice of

				overweight BMI $\geq 28 \text{ kg/m}^2$, desire to lose weight, fluent in Danish			1200 kcal/day . total of 10 hours of instruction from nutritionist
Christensen R, 2015	RCT	192	≥ 50 Mean age 62.5	50 or older, diagnosed OA based on clinical symptoms, including pain, and on standing radiographs. BMI $\geq 30 \text{ kg/m}^2$	Lack of motivation to lose weight, planned antiobesity surgery, total knee alloplasty, or receiving pharmacologic therapy for obesity	33	All participants went through 16 week intensive dietary weight loss intervention. Then group 1 was dietary, meeting with nutritionists weekly x 52 weeks. Group 2 was the exercise group. Daily 60 min workouts x 52 weeks. Group 3 was control group. Not given any instruction after 16 week dietary weight loss intervention
Riddle DL, 2013	Cohort	7,822 (4,796 + 3,026)	45-79	Aged 45-79, Radiographic knee OA, WOMAC pain scales of 4 or higher, & physical function scores 9 or higher	Planned TKA during follow up period, bilateral end stage OA, inflammatory arthritis,	860 (388 + 472)	None. Observation only. Patients were then divided into categories based on weight lost and weight gained

Outcomes Measure

All three articles focused on pain symptoms. The Western Ontario and McMaster Universities (WOMAC) was used to quantify pain levels of the participants.^{3,5} WOMAC is a healthcare questionnaire that evaluates pain, physical function, and stiffness. For this research, the 5 components of pain were evaluated; during walking, using stairs, in bed, sitting or lying, and standing. A Visual Analog Scale (VAS) for self-reported pain was also used.⁴ VAS is a continuous scale containing a horizontal and vertical line 100 mm in length anchored by 2 verbal

descriptors representing the extremes of each spectrum. Results are deduced by measuring from point 0 “No pain” to where the patient marked, giving results from 0-100. Change in weight from baseline was also recorded in all studies.

Results

The 2 RCTs and 1 cohort used in this research studied how pain symptoms were influenced by weight loss in obese adults with clinically diagnosed knee joint osteoarthritis. In the Bliddal study, there were 89 patients aged 36-90 with a mean age of 62.5 and a BMI ranging from 29 - 55 kg/m². They all had radiographic OA with a severity grade 2 or 3 on the Kellgren-Lawrence scale. Participants had a mean total WOMAC index at baseline of 39 mm and 89% were female.³ They were randomized into two groups; Low energy diet (LED) and control group. The LED group was provided with a formula diet consisting of 810 kcal/day for the first eight weeks, followed by 1200 kcal/day diet for 24 weeks, then another eight weeks of 810 kcal/day. They had a total of 44, 1.5 hour visits supervised by a dietitian, totaling 66 hours. The second group was given nutritional advice by the same dietitian, but instructed to consume 1200 kcal/day on their own. The control group had a total of 10 hours with the dietitian. At weeks 0, 8, 32, 36, and 52 weeks WOMAC scores were collected from all participants. Weight and body composition were also examined at the same intervals as independent predictors of pain symptoms related to OA. At the end of 52 weeks, the LED group had a mean weight change of -10.9 kg and the control group had weight change of -3.6 kg, resulting in a statistically significant difference with 95% CI and *p*-value of <000.1. Specifically evaluating the pain portion of the WOMAC scale, the LED group improved 7.7 mm, whereas the control group did not experience any reduction in pain, equaling a statistically significant group mean difference of

7.2 mm, equaling a *p*-value of 0.022 with a 95% CI.³ ARR for this study was 16.2% and NNT =6. There were no deaths or serious adverse events (SAE's) reported during the study. The most frequent adverse event in the LED group was constipation, reported in 5 patients (11%).

Table 2 - Weight change percentage and change in pain levels for each group

Variable	LED	Control	Difference in means	<i>p</i> -Value
Δ Weight (%)	-11.3	-3.7	7.5	<0.0001
Δ WOMAC pain (0-100 mm)	-7.7	-0.5	7.2	0.022

In the RCT by Christensen, there were 192 participants aged 50 or older, with a mean age of 62.5 with a diagnosed OA based on clinical symptoms and standing radiographs, and BMI \geq 30 kg/m². All 192 participants went through a 16-week intensive dietary weight loss intervention. After the 16-week intense diet, the participants were then divided into 3 groups; dietary, exercise, and control. The dietary group met weekly for 1 hour dietary sessions to discuss weight goals and progress, and were provided with weight loss shakes or snack bars. The exercise group exercised 3 days/week with a warm up phase of 10 minutes, a circuit-training phase of 45 minutes, and a cool down phase of 5 minutes.⁴ Exercises began supervised but slowly transitioned to home-based exercises. The control group was not given any instruction. After the 16-week intense dietary program plus 52 weeks of intervention, the dietary group had an average weight change of -11.0 kg, exercise group had an average of -6.2 kg, and the control group had an average of -8.2 kg. VAS pain scale showed a difference of -6.1 mm in the diet group, -5.6 mm in the exercise group, and -5.5 mm in the control group, resulting in no statistical

significance between the groups, with a p -value > 0.68 .⁴ Results are displayed below in table 3. There was p -value of < 0.03 across all groups in regards to decrease pain symptoms as related to decrease in weight with a 95% CI. 16 participants dropped out of the study. More participants dropped out from the control group (9), than the diet group (1) and the exercise group (6). Conservatively, the participants baseline studies were used for data analysis. No SAE's were reported. Mild adverse events included joint pain, back pain, and fatigue, with no clinically significant difference in data amongst these participants.⁴

Table 3 – Weight & pain symptom changes after 52-week intervention

Variable	Diet	Exercise	Control	p -Value
Δ Weight (Kg)	-11.0	-6.2	-8.2	<0.0001
Δ VAS pain (0-100 mm)	-6.1	-5.6	-5.5	> 0.68

The cohort study by Riddle and Stratford evaluated Osteoarthritis Initiative (OAI) and the Multicenter Osteoarthritis (MOST) datasets. OAI data at baseline and at 3 years were used, consisting of 4,796 participants. MOST data at baseline and at 30-months were used with 3,026 participants. For both studies, participants were required to be 45-79 years old, have radiographic evidence of tibiofemoral knee OA Kellgren-Lawrence grades 2 or higher, and WOMAC pain scale scores of 4 or higher. Both studies used the WOMAC pain scale to measure outcomes. At the end of the studies, participants were placed in five categories; $\geq 10\%$ body weight reduction, 9.9% to 5% body weight reduction, 4.9% reduction to 4.9% gain, 5% to 9.9% weight gain, and $\geq 10\%$ body weight gain. For this research, the outcomes of interest were the $\geq 10\%$ body weight reduction, 9.9% to 5% body weight reduction, and the control group with 4.9% reduction to

4.9% gain. The group with $\geq 10\%$ reduction showed an average change of 2.05 WOMAC pain scores and the 9% to 5% reduction showed 0.99, whereas the control group showed a 1.09 average change. These results showed a statistically significant difference between the $\geq 10\%$ weight reduction and the control group, with a p -value < 0.001 with a 95% CI.⁵

Table 4 – Change in pain scale for each weight change group

Weight Δ Category	Mean WOMAC pain scale Δ
$\geq 10\%$ reduction	2.05
9.9% to 5% reduction	0.99
4.9% reduction to 4.9% gain	1.09

Discussion

Obesity is a well-known risk factor for the development of knee joint OA. These articles evaluated whether or not losing weight helped to reduce the symptoms of knee joint OA after it had already developed. The greatest limitations of studying this clinical question are motivation to lose weight and compliance to weight loss intervention. Obesity is a growing healthcare epidemic. Millions of Americans struggle with their weight and repeatedly fail weight loss attempts. It is difficult to get a group of individuals to lose weight, and to lose a significant enough amount of weight to create clinical significance. Biddal's studied showed that weight loss due to an intense diet regimen over a 1-year studied significantly improved patient's pain and function per the WOMAC scale, with pain outcomes 2 times better than that of the control. Only 3 participants in the LED group reported non-compliance with the diet regimen.

Christensen's RCT placed all participants in a 16-week educational nutrition course, and then were divided into their intervention groups. At the end of the 1-year intervention study, there was no significant difference in the amount of weight lost between the groups. This shows that the 16-week educational course provided more benefit than anticipated. Because all groups lost weight, the researchers focused more on decreased pain symptoms as compared to weight loss regardless of what group the participants were in. Overall, the groups had an average decrease of pain symptoms by 15% and all had decreased weight. The cohort study by Riddle and Stratford demonstrated a dose-response relationship between body weight changes and changes in self-reported pain symptoms. Their data found that participants who lost $\geq 10\%$ body weight over a 3-year period had significant improvement of pain as compared to the reference category. They also found that a $\geq 10\%$ body weight gain had a significant increase in pain symptoms and worse function. Proving that weight gain has a negative impact on pain related to knee OA helps bolster the motive to get patients to lose weight in order to improve their symptoms. The biggest limitation for the cohort study was a 21% drop out rate, due to the length of the study.

Research has shown that losing weight will greatly improve symptoms related to knee OA, but the challenge in healthcare is motivating the patients. Both RCTs discussed the commonly reported excuse that patients with severe knee OA cannot lose weight because it is too painful to exercise. They showed that patients with knee OA could lose a substantial amount of weight with a diet regimen alone, and showed that participants could complete a 1-year exercise regimen with OA friendly exercises. Clinically, providers can use these studies to discuss weight loss options with patients and show that weight loss is possible for them.

Conclusion

This systematic review showed that weight loss in obese patients with pre-existing knee OA improved their knee pain symptoms. Out of the 3 articles examined, Bliddal's 1-year RCT with a control group and LED group was the most relevant and efficient study for the clinical question, allowing participants to lose weight in a relatively short period of time, however, the LED group does not guarantee that all participants will lose weight. This will alter results when comparing the two groups. Riddle's cohort study did not have any interventions, and therefore the result could be displayed and contrasted looking at the 2 variables, dividing results into groups based on how much weight they had gained or lost. These results were most specific for the independent and dependent variables being studied. In Christensen's RCT there were 2 intervention groups; diet and exercise. The average weight loss for the exercise group was less than that of the control group. This study focused on means of weight loss, rather than the affect weight loss had on pain symptoms. To observe more drastic results, future research may study obese patients with knee OA who are planning to have weight loss surgery. The type of study should be a cohort and results should be presented in the same manner as Riddle's cohort study, dividing patients into groups based on the percentage of body mass that was lost or gained, compared to their change in pain symptoms.

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