The Use of Prolotherapy for Chondromalacia Patella (Patellofemoral Pain Syndrome)

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ABSTRACT

Chondromalacia patella is a musculoskeletal pain disorder in which degeneration of cartilage underneath the patella can induce symptoms of pain, stiffness, and crepitus. If left untreated, it can often lead to knee osteoarthritis. Current treatments for chondromalacia patella (physical therapy, NSAIDs, etc.) are often ineffective and sometimes detrimental to the health of the knee. A proposed, alternative treatment currently provided to some patients is Prolotherapy, an injection technique used to stimulate the growth of new cells, including connective tissue. However, due to lack of research proving the treatment's efficacy, health care policies refuse to cover treatment costs. The purpose of this study is to expand upon findings in a previous study, providing empirical evidence regarding improvements of chondromalacia-related symptoms following Prolotherapy treatment. This retrospective cohort study followed the progress of 69 patients with chondromalacia patella who chose to receive Prolotherapy for their knees. A paired sample t-test was used to confirm changes in six indicators of the patient's condition (pain level at rest, pain level with normal activity, pain level during exercise, stiffness level, range of motion, level of crepitus) following Prolotherapy as measured in VAS scores. The results showed that there was a statistically significant improvement for all six measures ($p<0.01$). These findings indicate that symptoms of chondromalacia patella were reduced among patients who received Prolotherapy treatment and Prolotherapy should be considered as an alternative treatment. Further research is necessary to demonstrate the full efficacy and cost-benefit of the treatment, which may lead to the re-evaluation of health care policies regarding Prolotherapy use and coverage in regards to chondromalacia patella.

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KEYWORDS: Cartilage, chondromalacia patella, knee, osteoarthritis, patellofemoral pain syndrome, Prolotherapy.

Introduction

The incidence and prevalence of chronic musculoskeletal pain disorders (MSDs) in the United States is rising at an unprecedented rate. With the paradigm shift of diseases affecting the human population in developed countries switching from infectious diseases to non-communicable diseases, the prevalence of chronic MSDs is steadily increasing. The Global Burden of Disease identified low back pain, neck pain, and other musculoskeletal conditions as three of the top ten leading causes for years lived with disability worldwide.[1] According to a forthcoming report from the United States Bone and Joint Initiative[2], more than 78% of people age 18 years and older who reported having a disabling condition named a musculoskeletal disorder. The updated report also said more than one-half of the US population who live with a musculoskeletal condition experience decreases in both their quality of life and ability to perform activities of daily living. This was especially true for those who have back pain or arthritis and suffer from high rates of chronic pain, as well as disability. The prevalence rate of arthritis and joint pain nearly doubled from 10.7/100 in 1996-1998 to 20.8/100 in 2012-2014. Latest estimates indicate that more than 107 million pople per year experienced a musculoskeletal disease during 2012-2014, an increase of over 31 million since 1996-1998. This means over one-third of the population were affected by a musculoskeletal condition at least once per year in the 2012-2014 period and represents a 6% increase from 1996-1998 figures.

Chronic musculoskeletal pain disorders of the knee, in particular, debilitate individuals on various degrees of intensity, often leading to a decrease in physical functionality and an increase in sedentary lifestyles.[3] In the U.S., sedentary lifestyles and lack of exercise are some of the biggest factors leading to other non-communicable diseases, such as hypertension, cardiovascular disease, diabetes, and obesity.[4] One of the major consequences of these injuries is a significantly reduced health-related quality of life[5] and a decreased ability to do routine work.[6]

The cost of treating health issues caused directly and indirectly by knee injuries is growing. As of 2010, over 600,000 TKAs were being performed annually in the United States[7,8], far exceeding the 572,000 figure that had been projected for 2030 earlier in the decade.[9] By 2012, more than 670,000 total knee replacements had been performed in the United States, with corresponding aggregate charges of $36.1 billion.[8,10] The projected number of TKAs is now expected to increase 143% by 2050.[11]

In 2010 4.7 million individuals (3.0 million women and 1.7 million men) were living with a total knee replacement and these surgeries are expected to remain one of the most common elective surgical procedures in the coming decades.[12] The estimates for the number of adults with a TKA represent 4.2% of the population that is fifty years of age or older. Of those, 1.5 million were fifty to sixty-nine years old, refecting the trend that knee replacements are being done at a younger age.[8] Indeed, nearly 40% of TKAs are now being done on patients under age 65.[13]

There were also over 55,000 knee revision surgeries performed in 2010 in the US, with 48% of them being done on patients under 65 years. Estimated total costs associated with each revision TKA surgery are in excess of $49,000, which translates to an annual economic burden for revision knee OA surgery of $2.7 billion; this is for hospital charges alone. The projected annual economic burden of $13 billion projected by 2030[14] will surely be surpassed, just as the 2010 incidence of TKA was in 2010.

With the vast number of surgical procedures, radiological scans, pain medications, and other prescribed treatments for knee injuries, billions of dollars are being spent in the United States alone on these interventions, and these expenses are expected to steadily increase over the next fifteen years.[15,16] New data from the forthcoming edition of the United States Bone and Joint Initiative[2], substantiate this, as all-cause expenditures continue to be greatest for arthritis and joint pain, accounting for $626.8 billion in healthcare costs in 2012-2014. Overall, total average direct expenditures for persons with musculoskeletal diseases increased from $5,020 in 1996-1998 to $8,206 (2014 dollars), representing an increase of more than 60% in 2012-2014. Total per person direct medical care expenditures for arthritis and joint pain rose only 44% from $6,642 to $9,554. The mean direct all-cause cost per year per individual patient with a musculoskeletal disease has increased about 63%, rising from just over $5,000 to about $8,000 per person (in 2014 dollars) between 1996-1998 and 2012-2014.

However, due to the aging population and increasing number of individuals with musculoskeletal diseases, aggregate total direct all-cause expenditures to treat persons with a musculoskeletal disease for 2012-2014 was estimated at $882.5 billion—a whopping increase of about 130%. since the 1996-1998 time frame. Aggregate incremental medical cost is estimated to be $162.4 billion in 2012-2014, an 60% increase from the earlier time period. Incremental indirect costs attributable to musculoskeletal disease alone are estimated to amount to $159.2 billion. All-cause medical care expenditures averaged $11,502 for those with osteoarthritis and related disorders.[2]

The most common cause for knee pain is knee osteoarthritis (KOA)[3]; however, a precursor condition to KOA which is often overlooked is chondromalacia. Chondromalacia literally means the breaking down of cartilage. Chondromalacia patella, or patellofemoral pain syndrome (PFPS), occurs when the cartilage on the underside of the patella degenerates due to injury or misalignment of the knee joint, causing a softening and pain in the anterior portion of the knee.[17] This degeneration of cartilage can quickly lead to tracking issues of the patella and, if left untreated, can often lead to knee osteoarthritis.[18] Effective treatment of chondromalacia patella is usually difficult to manage due to the poor regenerative properties and complex physiology of cartilage.[19] Furthermore, traditional treatment options for chondromalacia patella (physical therapy, steroid injections, pain medications, and surgery) can indirectly cause more damage to the cartilage and surrounding tissue. For example, steroid injections are a commonly prescribed treatment for

treating musculoskeletal pain. However, repeated usage of steroid injections have been shown to decrease the musculoskeletal pain without healing the injury, often leading to an increased chance of induced tendon rupture.[20,21] The same can be said of treatment using NSAIDs (non-steroidal anti-inflammatory drugs), which have the mechanism to reduce inflammation and block pain receptors, but can also lead to further skeletal tissue damage.[22] Research shows that the optimal treatment for chondromalacia patella is still unknown[23], yet physicians continue to prescribe these traditional interventions, despite the lack of convincing evidence proving their efficacy.[24] Tragically, one-third of physically active patients diagnosed chondromalacia patella will be forced to permanently discontinue a sport or exercise due to knee pain.[25] These traditional treatments for chondromalacia patella often fail to repair or resolve these musculoskeletal injuries, which will maintain the high cost for health care expenditure and an increase in harm for the patient.[16-22]

Clearly, research should be conducted to find an alternative treatment solution for patellofemoral pain syndrome which is more effective at resolving the source of the problem. One intervention which may potentially induce improved symptoms and healing from chondromalacia patella is Prolotherapy, a treatment currently used to repair damaged connective tissues in relation to musculoskeletal pain disorders.[26] Prolotherapy is an injection technique intended to induce inflammation, the body's natural mechanism for healing, around the source of the musculoskeletal injury. Over time and several treatments, the procedure's goal is to induce the proliferation of new cells, repair the damaged connective tissue, and nearly resolve the injury. Recent research has indicated a certain efficacy in the treatment of Prolotherapy regarding ligament and tendon pathology.[27-30] In addition, research is now showing that Prolotherapy may be effective at regenerating new cartilage cells in vivo[26,27], making it a viable alternative to treating chondromalacia patella. Effective treatment of chondromalacia patella could reduce the overall incidence of knee osteoarthritis and many other knee related injuries.

However, research regarding Prolotherapy is inconclusive. Several studies have indicated that while it may be beneficial in treating some cases of musculoskeletal pain disorders, further research and investigation is necessary to indicate its full efficacy[31-33]. Due to this gap in research, there is a lack of coverage for Prolotherapy by a majority of health care providers. The U.S. Department of Health & Human Services' policy states that the "medical effectiveness of [Prolotherapy] has not been verified by scientifically controlled studies. Accordingly, reimbursement of these modalities should be denied on the ground that they are not reasonable and necessary as required by section 1862(a)(1) of the Act."[34] Consequently, patients who seek the treatment of Prolotherapy for chondromalacia patella, even after other interventions have failed, are refused coverage by major health care providers such as Medicare, Cigna[35], Aetna[36], and Blue Cross Blue Shield.[37] Patients must then pay fully for their Prolotherapy treatments, which may exclude or overly burden those who cannot afford to pay for the treatment. Therefore, further research should be conducted to determine whether patients have a significant improvement in symptoms and function when receiving Prolotherapy.

The goal of this study is to provide empirical evidence that the treatment of Prolotherapy would be effective in treating the condition of chondromalacia patella. It is an expansion of data from a previous outcome study on patients who received Prolotherapy for chondromalacia patella.[39] The current study objectively evaluates the difference in symptoms (level of pain, stiffness, range of motion, physical functionality, crepitus) in the patients from before and after the treatment via Visual Analog Scale (VAS) measurements. The difference in VAS measurements for each outcome will identify if there is a significant change in the patients' symptoms of chondromalacia patella (level of pain, stiffness, range of motion, physical functionality, and crepitus) due to Prolotherapy. The results of this study continue to lay the groundwork for further research and reevaluation of current policies regarding the treatment.

Methods

A retrospective cohort study was used to evaluate the effectiveness of Prolotherapy for chondromalacia patella. The target population of this study included human adults in the United States who were suffering from patellofemoral pain syndrome. The study population consisted of patients who were newly diagnosed with chondromalacia patella via physical examination; sought the treatment of Prolotherapy for their chondromalacia patella at Caring Medical & Rehabilitation Services in

Oak Park, Illinois; and completed the full protocol of Prolotherapy treatment as recommended by the ordering physician according to the severity of their condition. The patients received dextrose Prolotherapy to the knee, which included 15% dextrose, 10% Sarapin, 0.2% lidocaine, and sterile water. Patients typically received 30-40cc, including 5-10cc injected intraarticularly, per session. The treatment involved an average of 3-6 sessions per treatment, with each session 4-6 weeks apart, until completion of treatment. Before the first Prolotherapy session, patients were asked to provide a Visual Analog Scale (VAS)[39] score corresponding to each of six symptoms associated with chondromalacia patella, which were pain level at rest, pain level with normal activity, pain level during exercise, stiffness level, range of motion, and level of crepitus. These VAS scores were determined by the patient and documented by the nurse on a scale of 0-10, where 0 corresponds to no pain/no stiffness/full range of motion/full ability/no crepitus and 10 corresponds to constant pain/no stiffness/no range of motion/no ability/full crepitus. Following completion of the last Prolotherapy session, patients were again prompted to provide VAS scores for the same six symptoms. The data was collected for clinical use and then de-identified to protect the confidentiality of the patients and to reduce the risk for expectation bias by the principle investigator. This secondary data included patients who started and completed their treatment from February 2008 to September 2009. There were a total of 69 subjects which met study criteria for inclusion. Given a sample size consisting of the 69 subjects and assuming a standard deviation of 5, this study was able to show a difference of 2.1 for the change in VAS score after therapy with 80% power and a conservative alpha of 0.01 to allow for multiple comparisons.

Each patient file contained documented VAS scores of six outcome variables (pain level at rest, stiffness level, range of motion, pain levels during normal activities, pain level during exercise, level of crepitus) from before and after the Prolotherapy treatment. In this study, the utility of Prolotherapy for chondromalacia patella was assessed by the change in VAS scores of each of the six outcome variables documented from before the first session to their last session. A paired sample t-test was performed for each outcome variable to test for a change in VAS scores using Excel, an analysis software tool used for quantitative, biomedical studies.[40-42] Additionally, the patient file contained two key patient demographic characteristics (patient age at the time of treatment initiation and gender). Descriptive statistics were calculated for these variables to better characterize our sample population. Number of oral pain pills taken by the patients before and after the Prolotherapy treatment was also documented.

The data were additionally stratified by duration of time between initial knee pain and beginning of Prolotherapy treatment (patients treated within one year of initial pain, and patients treated after one year of initial pain) and by gender for comparative purposes. Duration of time between last session of treatment and data collection (in months), was also collected for each patient. No harm was placed on the subjects since they already completed the medical treatment at the time of the study. No control group was used in this study. Approval was obtained from the St. George's University Institutional Review Board prior to conducting this study.

Results

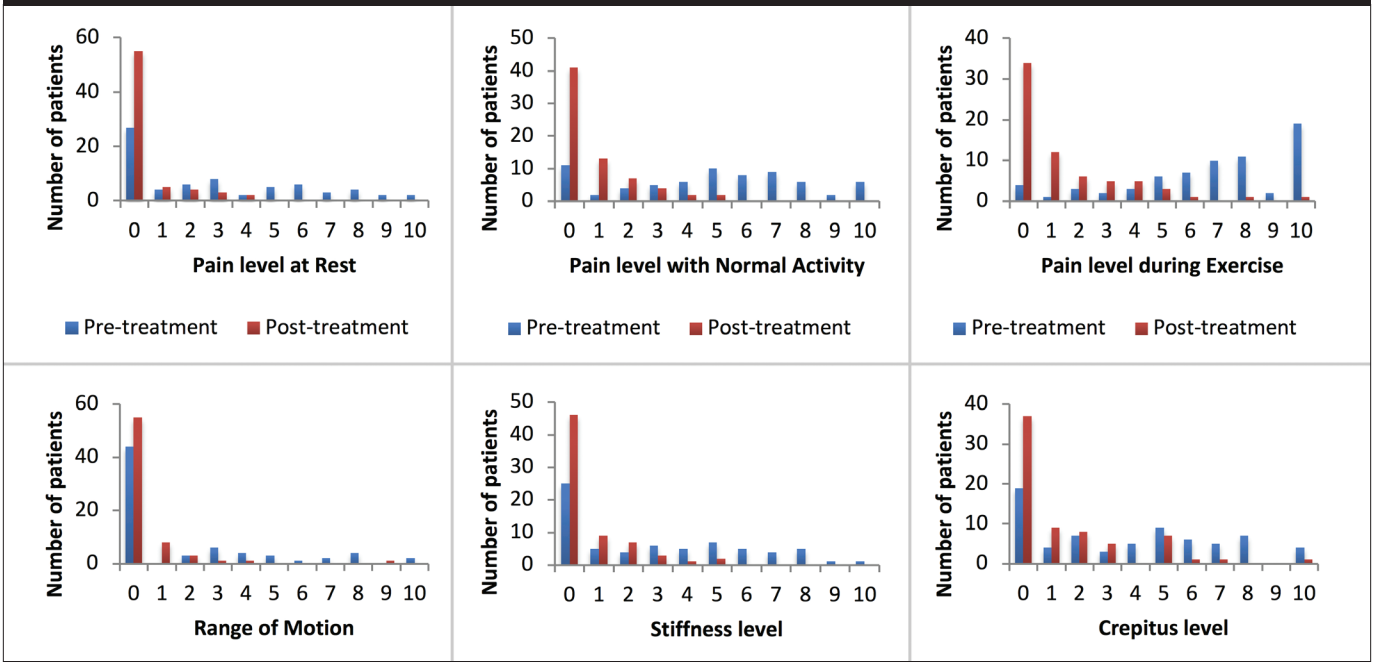
There were a total of 69 patients with chondromalacia patella who received the treatment of Prolotherapy in this study. Of the 69 patients, 52% (n=36) were male and 48% (n=33) were female with an average age of 47.2 years, ranging from 18 to 82. The average duration between initial observance of knee pain by the patient and Prolotherapy treatment was 21.7 months. The average duration between the patients' final Prolotherapy session and data collection was 14.71 months. (*See Table 1.*)

The distributions of all the patient VAS scores before and after the Prolotherapy treatment are listed in *Figure 1*. On average, patients reported significant decreases in pain

Table 1. Demographic characteristics of patients with chondromalacia patella who received Prolotherapy (n=69).

	Value
Age of patients [years], mean	47.4
Gender: Male	n=36
Gender: Female	n=33
Duration between initial knee pain & receiving Prolotherapy [months], mean	21.65
Treated within one year of initial pain	n=32
Treated beyond one year of initial pain	n=37
Duration between final Prolotherapy session and data collection [months], mean	14.71

Figure 1. Distribution of VAS scores for each symptomatic indicator before and after Prolotherapy treatment (n=69).



level at rest (2.9 v. 0.43; $p < 0.01$), pain level with normal activity (4.87 v. 0.83; $p < 0.01$), and pain level during exercise (6.81 v. 1.44; $p< 0.01$). Patients also reported significant improvements in range of motion (1.84 v. 0.43; $p < 0.01$), amount of stiffness (2.99 v. 0.68; $p< 0.01$), and levels of crepitus (3.75 vs. 1.42; $p<0.01$). (*See Table 2.*)

The mean VAS scores of patients stratified by duration of time between initial knee pain and beginning of Prolotherapy treatment and by gender resulted in similar outcomes when compared to the results of the entire study population. Patients who were treated within one year of initial pain and beyond one year of initial pain both reported decreases in pain level (at rest, with normal activity, during exercise) along with improvements in stiffness, range of motion, and crepitus. Improvements in these six, symptomatic indicators were also reported by both males and females. (*See Tables 3 & 4.*) Prior to the Prolotherapy treatment, 29 (42%) patients reported taking at least 1 pill of pain medication; after the Prolotherapy treatment, 3 (4%) patients reported taking at least 1 pill of pain medication.

Table 2. Self-reported VAS scores of chondromalacia-related symptoms before and after Prolotherapy treatment (n=69).

	Pre-treatment Mean	Post-treatment Mean	Difference	P-value
Pain level at rest	2.9	0.43	2.47	<0.01
Pain level during normal activity	4.87	0.83	4.04	<0.01
Pain level during exercise	6.81	1.44	5.37	<0.01
Range of motion	1.84	0.43	1.41	<0.01
Stiffness level	2.99	0.68	2.31	<0.01
Crepitus level	3.75	1.42	2.33	<0.01

Discussion

The results of this retrospective cohort study illustrated that patients with chondromalacia patella who received Prolotherapy reported a significant decrease in their levels of pain at rest, normal activity, and exercise, in addition to an improvement of range of motion, decrease in knee stiffness, and reduction in crepitus. The differences in VAS means scores for each of the six outcome variables were shown to be highly statistically significant, with a p-value of less than 0.01 for each variable. Additionally, the number of patients who took oral pain medications prior to the Prolotherapy (29 patients) decreased by 26% in comparison to the number of patients who took oral pain medications after the completion of the

Table 3. Gender VAS scores before and after Prolotherapy treatment.

	Pre-treatment Mean	Post-treatment Mean	Difference	P-value
Male (n=36)				
Pain level at rest	2.25	0.33	1.92	<0.01
Pain level during normal activity	3.78	0.64	3.14	<0.01
Pain level during exercise	6.17	1.33	4.84	<0.01
Range of motion	1.19	0.33	0.86	<0.01
Stiffness level	2.67	0.36	2.31	<0.01
Crepitus level	3.39	1.42	1.97	<0.01
Female (n=33)				
Pain level at rest	3.6	0.55	3.06	<0.01
Pain level during normal activity	6.06	1.03	5.03	<0.01
Pain level during exercise	7.53	1.56	5.97	<0.01
Range of motion	2.55	0.55	2	<0.01
Stiffness level	3.34	1.03	2.31	<0.01
Crepitus level	4.15	1.42	2.73	<0.01

Table 4. Duration between initial pain and Prolotherapy (VAS scores before and after Prolotherapy treatment).

	Pre-treatment Mean	Post-treatment Mean	Difference	P-value
Treated within one year of initial pain (n=32)				
Pain level at rest	3.59	0.66	2.94	<0.01
Pain level during normal activity	4.94	0.56	4.37	<0.01
Pain level during exercise	6.87	0.74	6.13	<0.01
Range of motion	2.22	0.41	1.81	<0.01
Stiffness level	3.1	0.55	2.55	<0.01
Crepitus level	3.13	0.81	2.32	<0.01
Treated beyond one year of initial pain (n=37)				
Pain level at rest	2.3	0.24	2.06	<0.01
Pain level during normal activity	4.81	1.05	3.76	<0.01
Pain level during exercise	6.76	2.03	4.74	<0.01
Range of motion	1.51	0.46	1.05	<0.01
Stiffness level	2.89	0.78	2.11	<0.01
Crepitus level	4.3	1.95	2.35	<0.01

treatment (3 patients). This indicates that the decrease in chondromalacia-related symptoms were not due to pain relief medications, which may have disguised the effects of Prolotherapy. This may also illustrate that Prolotherapy reduces the need for oral pain medications in patients suffering with symptomatic chondromalacia patella.

Most physicians and health care officials regard the efficacy of Prolotherapy as inconclusive.[31-33] For this reason, current United States policy withholds the right of deeming Prolotherapy a designated treatment for conditions such as chondromalacia patella.[34] Consequently, major health insurance providers do not cover the costs of Prolotherapy. The results of this study, however, illustrate that patients with chondromalacia patella reported statistically significant improvements in major symptoms (such as pain level at rest, pain level with normal activity, pain level during exercise, stiffness, range of motion, and crepitus) when receiving Prolotherapy. These results were seen in patients with varying gender and duration of time between initial pain and treatment. In addition, the patient age in this study ranged from 18 to 82, which may illustrate the generalizability of Prolotherapy to the majority of the population. Since traditional treatments for patellofemoral pain syndrome have often been identified as inefficient[19], harmful[20,21], and overall not optimal[22], governmental funding should be allocated for further research regarding the efficacy and cost of Prolotherapy. Results of this research should promote re-evaluation and analysis of current health care policies regarding Prolotherapy.

A major limitation of this study was the lack of a control group, for it is impossible to tease out effects of Prolotherapy with temporal trends without a comparison group who did not receive the treatment but were given the traditional treatment for chondromalacia patella. Lack of MRI documented diagnosis of chondromalacia

patella may also be a limitation to this study. Although the patients were diagnosed via physical examination, MRI scans would more accurately diagnose chondromalacia patella, lowering the risk of obtaining subjects under false positive or false negative results. The MRI could also indicate conditions other than chondromalacia patella which may be affecting the patient's symptoms. The stratification of age was not considered in this study due to the limited sample size, yet it would be beneficial to evaluate the effect of this variable in more detail for future studies. Overall, further research must be done to investigate the actual role Prolotherapy plays in regeneration of cartilage in patients with chondromalacia patella. The ideal study would be a randomized control trial, in which an equal number of patients, who were diagnosed via MRI and shared similar demographic and medical factors, received the treatment of Prolotherapy or the gold standard treatment. Confirmation of results would be confirmed via MRI scans.

One of the strengths of the study was the use of the VAS system.[39] Patients were able to assess their progress or lack of progress on a standardized scale for measuring pain intensity level, stiffness level, range of motion, and level of crepitus. This helped to quantify the patient responses for analysis and comparison. In addition, the patients paid full price for treatment, which would increase the accuracy of VAS scores provided at each visit, reducing the overall risk of reporting bias. To decipher whether the effects of Prolotherapy varied upon duration of time between initial pain and time of treatment, patients were stratified by those who obtained treatment within one year of initial pain (n=32) and those who obtained treatment beyond one year of initial pain (n=37). The results illustrated that patients observed significant improvements regardless of duration between initial pain and treatment ($p<0.01$). These finding might suggest that Prolotherapy could be effective at treating both acute and chronic cases of chondromalacia patella. Another variable which was considered in this study was that of gender. Analysis was conducted to determine whether the improvements of Prolotherapy were more dominantly seen in one gender versus the other. There were fairly similar groups of males (n=36) and females (n=33) for comparison. The results illustrated that both men and women observed a significant improvement in symptoms after the Prolotherapy without much difference between gender ($p<0.01$). This may generalize the potential benefits offered by Prolotherapy to both genders.

In summary, the outcomes of this study illustrated that Prolotherapy may be an effective treatment for reducing the symptoms of chondromalacia patella. The observed decreases in symptoms of patients who received Prolotherapy were shown to be highly significant ($p<0.01$). The patients in this study who received Prolotherapy improved in overall level of pain, function, and mobility in the case of chondromalacia patella. These improvements were seen in varying durations of initial pain and treatment and gender. Improvements observed with Prolotherapy were seen in patients of all ages, making the potential benefits of Prolotherapy generalizable to the majority of the U.S. adult population. Since traditional treatments for this condition are often ineffective and sometimes detrimental to the health of the knee, serious consideration should be placed on using Prolotherapy as a first-line treatment for chondromalacia patella. An illustrated improvement in patient pain level, stiffness, physical activity, and range of motion would suggest the need for further research in both the efficacy and cost-benefit of using Prolotherapy for patellofemoral pain syndrome. However, if Prolotherapy proves to be more effective and less expensive than traditional treatments for chondromalacia patella, then health care policy should re-evaluate the use and coverage of Prolotherapy in the condition of patellofemoral pain syndrome. Implementing a more effective and less expensive treatment would reduce the overall prevalence of MSDs in the U.S., save future health care costs, and improve the overall health and well-being of individuals struggling with musculoskeletal pain. ■

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