CE

1.5 ANCC Contact Hours

Effectiveness of Platelet-Rich Plasma in the Management of Knee Osteoarthritis in a Rural Clinic

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BACKGROUND: Osteoarthritis (OA) is a degenerative disease causing decreased mobility. Use of autologous platelet-rich plasma (PRP) provides a reparative alternative in the management of OA.

METHODS/PURPOSE: This study assessed effectiveness of nurse practitioner-injected PRP to manage knee OA in a rural setting.

RESULTS: Twenty patients were followed for 1 month after PRP treatment. Knee function and pain levels were assessed using a knee function score (Knee Injury and Osteoarthritis Outcome Score Physical Function Short Form [KOOS-PS]).

CONCLUSIONS: Overall, the 20 patients who participated in this study experienced significant improvement in knee function scores, decreased pain, and decreased use of pain medications.

Osteoarthritis (OA) is a chronic degenerative disease with progressive destruction, thinning, and wearing of articular cartilage, ultimately causing chronic pain (Zhu et al., 2013). The Centers for Disease Control and Prevention ([CDC]; 2015) reports that OA is the most common form of arthritis affecting 13.9% of adults 25 years and older and 33.6% (12.4 million) of those 65 years and older in 2005.

In OA-related articular cartilage damage, the major issues for clinicians are pain control and management. Articular cartilage damage and pain are usually caused by sports injuries, accidental trauma, or aging (Zhu et al., 2013). In the absence of a cure, current treatments are aimed at reducing pain and improving joint function. Clinical management of pain in OA is often limited to the use of oral analgesics such as anti-inflammatory medications and opiates (Chang et al., 2014). Intra-articular corticosteroid injections have been widely used in the management of symptomatic knee OA, but its effectiveness is limited to the short term (McAlindon et al., 2014). Surgery may be indicated if pain is debilitating and/or if the patient is experiencing major limitations in walking, working, or sleeping (Henriksen, Hansen, Klokker, Bliddal, & Christensen, 2016). Other recommended nonpharmacological interventions include patient education and self-management, exercise, weight reduction, walking support (crutches, bracing, shoe insoles), acupuncture, local cooling/heating, and intra-articular injections with blood products (Ayhan, Kesmezacar, & Akgun, 2014).

Oral analgesics, steroidal injection, and surgical interventions bring about temporary relief from pain but do little to reduce joint cartilage degeneration (Spaková, Rosocha, Lacko, Harvanová, & Gharaibeh, 2012). Articular regeneration is limited because of its isolation from the systemic regulation and lack of vascularization leading to low healing potential (Filardo et al., 2011).

Several studies have been conducted to investigate new reparative methods of stimulating cartilage regeneration that subsequently improve function of the affected joints and decrease pain. In tissue biology, intra-articular injections with autologous blood products, in particular platelet-rich plasma (PRP), have shown promising positive results in OA treatment (Jang, Kim, & Cha, 2013; Marmotti et al., 2015). Platelet-rich plasma is a product rich in growth factors (GFs) that can stimulate healing and regeneration of the cartilage. It is simple and low cost and provides a minimally invasive way to obtain a concentration of GFs that can be used to reduce inflammation, improve joint function, and decrease pain (Ayhan et al., 2014). Importantly, the use of autologous blood products eliminates the possibility of transfusion reactions and disease transmission (Di Matteo, Kon, & Filardo, 2016).

The use of autologous products, particularly PRP, for managing pain and improving joint function, is a growing field in orthopaedics. Platelet-rich plasma works by focusing on the introduction of GFs to maximize

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healing of the bone and soft tissues (Zhu et al., 2013). It is one of the autologous products that has been studied and utilized in OA managements since 1970 due to its regenerative and anti-inflammatory properties (Marmotti et al., 2015; Zhu et al., 2013). Despite it being safe and inexpensive to administer, PRP has not become a mainstay therapeutic intervention for the treatment of OA in primary practice (Ayhan et al., 2014).

Platelet-rich plasma is obtained by centrifuging autologous blood to obtain a volume of plasma with a platelet concentration above baseline (Gobbi, Karnatzikos, Mahajan, & Malchira, 2012). Platelets contain more than 30 bioactive proteins and GFs, which regulate key processes in tissue repair including chemotaxis, migration, recruitment, proliferation, and differentiation of cells involved in tissue regeneration (Filardo et al., 2011, 2013). In an injury, platelets begin actively secreting these proteins within 10 minutes of clotting, with more than 95% of the presynthesized GFs secreted within 1 hour. After the initial burst of GFs, the platelets synthesize and secrete additional GFs (Engebretsen et al., 2010; Kilincoglu, Yeter, Servet, Kangal, & Yildirim, 2015). Platelet-rich plasma also contains proteins such as fibrin, fibronectin, vitronectin, and thrombospondin, which are known to act as cell adhesion molecules and are important for the migration of osteoblasts, fibroblasts, and epithelial cells (Schliephake, 2002). These are the biological properties of platelets that enable PRP to stimulate and enhance articular regeneration and healing, hence improving joint function and decreasing pain levels.

In a systematic review and meta-analysis, Chang et al. (2014) found that PRP injections in patients with knee degenerative pathology improved function from basal evaluations. However, participants with lower degrees of knee cartilage degeneration benefited more from PRP injections than those with advanced OA. Similarly, Kon et al. (2010) studied the short-term efficacy of PRP in patients who received a total of three injections at 3-week intervals and found a reduction in pain as measured by the visual analog scale at 6 and 12 months. However, the affected knee symptoms became worse after 24 months, even though they were still better than those at baseline.

The efficacy of PRP has been compared with hyaluronic acid (HA), which enhances viscosity and elastic nature of the synovial fluid, hence acting as a shock absorber during rapid joint movements. It also has anti-inflammatory, anabolic, and analgesic effects in OA (Ayhan et al., 2014). In a 12-month study, Raeissadat et al. (2014) found that PRP use is more efficacious than HA injections in reducing pain symptoms and improving quality of life. In a comparison of PRP and HA, Sánchez et al. (2014) noted that PRP had superior, significant results in improved knee function and decreased pain over 24 weeks. Sanchez et al. emphasized that PRP had a higher safety profile than HA.

The use of PRP, in general, has not been standardized, and there are a range of protocols differing by the number of injections and time interval between injections (Di Matteo et al., 2016; Engebretsen et al., 2010). Because of this variance in time to determine positive results from PRP, more studies are needed to determine the optimal therapeutic protocol for PRP.

PRP in Rural Settings

Because of the cost of pain management of OA in a rural setting, where a greater percentage of rural residents with arthritis are of lower socioeconomic status than their urban counterparts (Lutfiyya et al., 2013), cheaper pain treatment modalities are needed. Therefore, exploring alternative pain management modalities such as PRP is crucial in the rural setting. The health of rural residents is confounded by factors that include low education and high poverty levels, being uninsured and underinsured, unemployed and underemployed, and the geographical distance to travel for healthcare (Logan, Guo, Dodd, Muller, & Riley, 2013). People with arthritis in rural settings are at greater risk for healthcare deficits than people in urban areas (Lutfiyya et al., 2013).

Rural residency is a predictor of a high prevalence of arthritis among U.S. adults 45 year and older (Lutfiyya et al., 2013). Moreover, the rural population has a large number of farmers who are vulnerable to a range of musculoskeletal disorders such as OA of the hip and knees (Osborne et al., 2012). The CDC asserts that people in rural counties use more prescription pain killers and are nearly twice as likely to overdose on prescription pain killers as compared with people in urban areas (CDC, 2011).

This project investigated the effectiveness of PRP in OA pain management as an alternative to pharmacological treatment. As a conservative therapeutic intervention, PRP is a feasible alternative for the management of chronic pain related to OA for rural residents. Platelet-rich plasma injections require only basic supplies and a centrifuge, which are common in most healthcare clinics, including rural clinics.

Methods

PRP Preparation and Injection

Platelet-rich plasma was offered by the nurse practitioner who was trained in the preparation and administration of PRP to large and small joints and trigger points. Upon agreeing to PRP treatment, two 8-ml samples (in specimen tubes) of the patient's blood were obtained through peripheral venous access. The blood sample was immediately centrifuged for 20 minutes at 3,400 rpm to separate the platelets from other blood products. The centrifuged blood is usually stratified into three layers in the specimen tube. The base, named the red layer, contains erythrocytes; the middle layer contains leukocytes and the inflammatory cytokines; and the top, or yellow layer, is filled with plasma, platelets, and GFs (Lopez-Vidriero, Goulding, Simon, Sanchez, & Johnson, 2010). This process is done under sterile conditions. The platelet layer is drawn from the specimen tube and then injected into the intra-articular space of the knee joint with an appropriately sized needle. Immediate hemostasis is achieved by applying pressure.

Postprocedure care for participants includes limiting activities for 24 hours after injection and use of cold therapy in case of pain at the injection site. Patients have permission to continue with their regular pain medications, excluding anti-inflammatories, for the first

48 hours, with the recommendation to reduce or stop their pain medication as their OA symptoms resolves.

Target Population

This project was conducted in a rural setting; the target population was adults older than 18 years who presented to a primary care clinic for the treatment and management of OA. Patients who present with OA often requested steroidal injections, nonsteroidal anti-inflammatory drugs, and/or opioid prescriptions. The rural clinic was able to offer PRP as an alternative treatment of OA. However, very few patients were aware of PRP treatment as an alternative treatment option with the potential of improving knee function, decreasing pain levels, reducing the use of pain medications, and potentially eliminating or delaying the need for knee surgery.

Patients who presented with and met the diagnostic criteria for OA were invited to participate in this project. This study was approved by the institutional review board, and informed consent of all participants was obtained. Knee Injury and Osteoarthritis Outcome Score Physical Function Short Form (KOOS-PS) scores were provided to patients by the clinic staff. Patients were given additional copies of the KOOS-PS, which they were asked to complete and return 2 weeks and 1 month following the injection. The PRP procedures followed were those recommended by Lopez-Vidriero et al. (2010).

The KOOS-PS ("What is the KOOS-PS," 2016) is a short version of the original KOOS questionnaire, which is as a measure of physical function derived from activities of daily living and sports/recreation. Patients were to report the degree of difficulty incurred within the past week on rising from bed, putting on socks, rising from siting, bending to the floor, twisting on injured knee, kneeling, and squatting. These seven items are scored on a 5-point Likert scale (none, mild, moderate, severe, and extreme) scored from 0 to 4. The individual categories with a Likert scale are summed up and matched against a nomogram scale. The scoring of KOOS-PS is bidirectional, from no difficulty (0) to extreme difficulty (100) or from extreme difficulty (0) to no difficulty (100).

The KOOS-PS has shown adequate internal consistency and test–retest reliability for patients with OA, particularly those receiving interventions such as intra-articular injections and physical therapy (Collins, Misra, Felson, Crossley, & Roos, 2011; Perruccio et al., 2008).

In addition to the KOOS-PS scale, a questionnaire with a Numerical Rating Scale (NRS) was administered to evaluate overall pain levels before and after treatment (see Figure 1). The scale was a rating of "0" for no pain up to "10" for the most severe pain. This NRS questionnaire also enquired about the number of treatments received, pain level at each of the intervals, potential changes in pain medication use following injection, and willingness of participants to continue to receive additional PRP injections.

Demographic data included gender, age, and body weight. Repeated-measure analyses of variance (ANOVAs) were used to calculate significance of KOOS-PS scores at each measurement interval, followed by paired *t* tests. A chi-square test was utilized to calculate the relationship of independence between the willingness of participants to travel to a different, further location to seek and receive PRP treatments. Finally, the Wilcoxon test was used to calculate significant relationship between the NRS scores between the measurement intervals.

Please fill out the following question to the best of your knowledge

1. How many PRP treatments have you received? _____

2. Rate your pain level in a scale of 0-10 (0 -being no pain and 10 being the highest pain)

   A. Before PRP_____ 0 2 4 6 8 10

   B. 2 weeks after PRP___ 0 2 4 6 8 10

   C. 1 Month after PRP__ 0 2 4 6 8 10

3. Have you reduced or stopped taking your regular pain medication since PRP injection?

   A. Yes_____ B. No_____

4. If PRP was not available in this clinic, will you drive over 50 miles to get the injection somewhere else?

   A. Yes_____ B. No_____

5. What pain medication or additional pain medications have you taken?

   _____

6. Are you willing to continue with PRP treatment

   A. Yes_____ B. No_____

Figure 1. Numerical Rating Scale. PRP = platelet-rich plasma.

Results and Findings

A total of 20 participants (11 females [55%] and 9 males [45%]) were recruited to participate in the study; participants ranged in age from 35 to 83 years, their mean age was 48 years, and they had a mean body mass index of 31.6. Participants received varied numbers of PRP injections, with 60% of participants receiving only one injection. No major adverse events were reported during the period of study. One participant failed to complete the baseline survey, and one failed to complete the 1-month survey. All others completed both of these surveys. One patient indicated that PRP had not provided *any* benefit after one treatment and his knee symptoms had gotten worse.

Overall, participants' mean pain level on the NRS showed improvement from 8.53 before treatment to 6.05 and 4.32 at 2 weeks and 1 month, respectively. A Wilcoxon test found a significant difference ($Z = -3.66$, $p < .001$), indicating decreased pain as compared with before and after treatment. A Wilcoxon test comparing NRS scores at 2 weeks and 1 month found a significant difference ($Z = -2.68$, $p < .007$), indicating NRS scores at 1 month were lower than those at 2 weeks. Finally, a Wilcoxon test between NRS scores before treatment and at 1 month also indicated there was a significant difference ($Z = -3.76$, $p < .001$), with NRS scores at 1 month lower than the pretreatment scores. These results indicated that overall knee pain scores progressively decreased at each measurement interval, with the greatest improvement at 1 month (see Figure 2).

Overall, patients reported an improvement in knee function scores as measured by the KOOS-PS. A one-way repeated-measures ANOVA was significant, $F = 15.67$, $p < .001$. A paired t test revealed that KOOS-PS scores increased significantly from before treatment ($M = 39.42$, $SD = 23.38$) to KOOS-PS scores at 2 weeks ($M = 62.38$, $SD = 19.6$) and KOOS-PS scores at 1 month ($M = 70.5$, $SD = 21.28$) (see Figure 3).

Although all functional activities showed improvement, the greatest improvement in functionality was for putting on socks/stockings and bending to the floor. Individuals reported the lowest functionality gains in squatting, which were the highest scores at baseline and showed the least improvement.

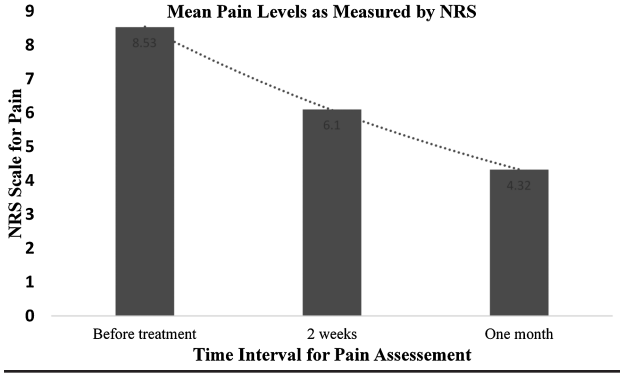

Figure 2. Participants' mean pain levels as measured by the NRS before treatment, at 2 weeks, and at 1 month. NRS = Numerical Rating Scale.

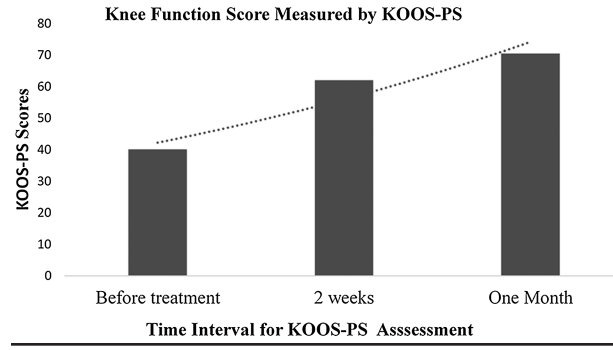

Figure 3. With 20 participants, mean KOOS-PS scores were calculated before treatment, at 2 weeks, and at 1 month post-PRP treatment. KOOS-PS = Knee Injury and Osteoarthritis Outcome Score Physical Function Short Form; PRP = platelet-rich plasma.

When participants were surveyed whether they would continue with the treatments, 18 (90%) indicated that they will continue with PRP treatment. Sixteen participants (80%) indicated that they were willing to travel to a distant location to get PRP treatment if it was not offered in the local rural clinic.

In this study, 55% of the participants responded that they routinely took narcotic pain medications for pain related to OA whereas 30% of participants took nonnarcotic pain medications at intake. One of the objectives of this study was to assess whether participants reduced or stopped the utilization of pain medications after treatment. Interestingly, at 1 month after the injections, 12 participants (60%) indicated that they had either reduced or stopped taking pain medications.

Discussion

The use of PRP provides a regenerative and reparative treatment alternative for OA. In recent years, the use of autologous blood products, especially PRP, has been extensively used in specialty medicine such as orthopaedics and sports medicine. A number of studies have indicated that PRP will improve joint function and reduce OA symptoms. Its use may delay or avoid the need for invasive surgical procedures for degenerative joints (Filardo et al., 2011; Shen, Yuan, Chen, Xie, & Zhang, 2017).

This study's findings were consistent with those of previous studies that evaluated knee function at 6 and 12 months. Similarly, Filardo et al. (2011) evaluated effectiveness of PRP in the treatment of degenerative lesions of the knees showing progressive improvement despite different evaluation times. It is important to note that there has been no set standard time for evaluation of effectiveness of PRP in the treatment of OA symptoms.

This study demonstrated early functional improvement and a decrease in OA knee symptoms and pain at 2 weeks and 1 month with PRP treatments. These are overall benefits that are not exhibited when corticosteroids and HA are used in OA treatment (Shen et al., 2017). Even though PRP treatments are effective early in the course of treatment, their most important benefit is the subsequent long-term resolution of OA symptoms.

Currently, there are no established standard time frames for determining PRP effectiveness in the treatment of OA. Even though assessments in this study were at 2 weeks and 1 month, similar results have been found in other studies that were conducted at longer time intervals. In this study, the greatest increase in functionality occurred in the first 2 weeks following injection, although additional functional gains were made during the next 2-week period. The greatest increase in functionality occurred for putting on socks and bending to the floor. The smallest functionality gains were in the category with the highest mean score at baseline, which was squatting.

Introduction and utilization of PRP treatment of musculoskeletal complications are particularly important in the rural setting, as rurality in itself is a risk factor for multiple musculoskeletal complications including OA (Lutfiyya et al., 2013). Platelet-rich plasma provides a readily available treatment option for rural patients due to low cost and because special equipment is not needed. The long-term efficacy of PRP makes it the better alternative for rural patients as it can reduce clinic visits, travel time, and medical expenses; it can also alleviate or delay the need for surgical intervention.

The introduction of PRP in managing OA in a rural setting can decrease use of prescription and nonprescription pain medications. This study found that 60% of the respondents indicated that they had either stopped or decreased their pain medication use. This is important due to increased use of pain medications in the rural setting (Lutfiyya et al., 2013).

Limitations

Unlike other research related to knee OA, this study was conducted without the use of imaging studies such as knee radiography and magnetic resonance imaging for the diagnosis and assessment of the severity level before treatment. The need for imaging originates from previous reviews, which contend that PRP has shown better improvement in knee function in patients with early OA than in those with moderate to severe OA. However, radiographic evidence in other studies indicates that discernable changes do not occur until 2 months after injection, which was beyond the scope of this study (Görmeli et al., 2017). An additional limitation was the lack of a placebo control group. The limited sample size and nonrandomized study design limited the power of this study but provided evidence that additional research into the use of PRP in a rural clinic is warranted.

Conclusion

This project highlights the need to give attention to chronic health problems—in particular pain management—in rural areas. This study also underscores the difficulty that rural residents have when accessing healthcare services and health providers, especially for chronic pain management (Tollefson, Usher, & Foster, 2011). Furthermore, rural and nonrural differences in health-related quality of life can be accounted for by low income, higher body mass index, and increased prevalence of joint diseases and injuries (Miles, Proescholdbell, & Puffer, 2011). For these reasons, the use of PRP in a rural setting for the treatment of OA will be particularly useful. Platelet-rich plasma not only is an alternative to pain management for OA in rural patients but can also help improve the quality of life. Additional studies are needed to determine the best protocol for PRP preparation, optimal concentrations, and composition. Further research is needed to assess and standardize the time frame for expected optimal clinical improvement.

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