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Implication of Covid-19 Infection on PRP Extraction in a Patient Suffering from Knee Osteoarthritis

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Abstract

Background

Knee osteoarthritis (KOA) is one of the most prevalent degenerative diseases that cause pain and disability. None of the currently available treatments reverses or heals the degenerative nature of this condition. There were many research studies on the efficacy of PRP therapy in early KOA patients. However, there was no clinical study on its extraction or administration in a COVID-19 patient with KOA.Hence, the main objective of this observational study was to analyse the implication of COVID-19 infection on PRP extraction along with Red Blood Cell Distribution Width (RDW) and platelet count levels.

Methods & Findings

We present a case report of knee osteoarthritis administered with two ultrasound-guided Platelet-Rich Plasma (PRP) injections pre and post covid-19 infection.
As the patient was affected with COVID-

Conclusion

As COVID-19 infection affects the lungs, there was an increase in hematocrit values, leading to difficulty in plasma separation. Furthermore, there was an elevated level of RDW with the change in platelet count.

Keywords

PRP therapy; Knee Osteoarthritis; COVID-19; RDW

Introduction

Knee osteoarthritis (KOA) is ubiquitous in 10% of males and 13% of females among the elders due to a gradual increase in ageing, obesity, and life expectancy [1]. It was estimated that this condition could affect over 10% of the population across the world [2,3], with a lifetime risk of 45% [3,4]. Since none of the currently existing treatments reverses or heal the degenerative nature of this condition [6];there has been considerable attention on non-surgical regenerative injections.Unlike other conservative treatments, Regenerative cell therapy uses the anti-inflammatory and healing properties of a patient's cells to heal the inflamed and painful joint area. [6]. Platelet Rich Plasma (PRP) therapy, one of the types of regenerative cell treatment, is being evaluated to relieve knee osteoarthritis symptomatic pain and inflammation [7,8].

Autologous PRP mainly consists of platelets with varied bioactive substances, including growth factors, TGF-b, VEGF, IGF1, alfa granules, etc. It plays a significant role in repairing the tissues naturally and promotes tissue regeneration [9].PRP therapy has several advantages over other treatments concerning non-invasiveness, non-immunogenic, cost-effectiveness, and relatively safe [10].Furthermore, patients undergoing PRP treatment revealed no adverse side effects [11]. Some publications have even stated that PRP therapy could be a promising alternative for knee osteoarthritis treatment [12–14]. Although regenerative treatment was reported to be safe in patients with moderate-to-severe KOA for 12 months post-COVID-19 vaccination, there was no clinical study on the effect of PRP immediately after COVID-19 infection [15].

Patients with COVID-19 were found to be associated with thrombocytopenia (lower platelet count in the blood).The reason for this lower platelet count was reported to be the utilisation of platelets in forming pulmonary thrombito prevent the occurrence of viremia through the bloodstream [5]. It was anticipated that damaged endothelium would result in platelet activation, thrombi formation, and platelet consumption [19]. There was a significant increase in venous thromboembolism among people hospitalised due to COVID-19 infection [20].Furthermore, this study reported the Red Blood Cell Distribution Width (RDW) level and thrombocytopenia rates since low platelet count was estimated to be about 5-41.7% in patients with COVID-19 [19]. As there was a drop in platelet count, the main objective of this current case study was to describe the implication of COVID-19 infection on PRP preparation, especially in a patient suffering from KOA.

Case Presentation

An Irish man, 45 years old, presented to a Medica Pain Management Clinic with a grade-2 left knee osteoarthritis diagnosis, with limited range of motion and pain onset around five months before. He had no knee traumas in the last year. As a diabetic patient, he consumed only a non-dairy, gluten-free diet. The patient underwent a complete KOA rehabilitation program and intra-articular injections of corticosteroids and hyaluronic acid with no significant outcomes. In addition, Naproxen(1000 mg) and Neurofen (non-steroidal anti-inflammatory drugs (NSAIDs) (400 mg) were consumed twice daily. Healso had no significant improvement in pain for the past 3 months.

Hence, the patient visited the Medica Pain Management clinic for a consultation on possible non-surgical treatments for his left knee pain, where he was recommended platelet-rich plasma injections. Both written information and proper education were provided regarding PRP and its use within knee osteoarthritis, including the possible risks involved. The patient was already diagnosed with grade-2 knee osteoarthritis and failed conservative treatments, so he was assessed as a suitable candidate for ultrasound-guided PRP injections. Formal written informed consent was received from the patient before the commencement of treatment.

Treatment

PRP Preparation& Administration

The PRP was extracted from the 15ml ofthe patient's peripheral blood via swing centrifugation as per the established protocol of the Y-Cell Bio-kit(Y-cell Bio-kit for PRP extraction: http://www.ycellbio.com/bbs/content.php?co_id=ycellprp_en) and administered intra-articularly using ultra-sound guidance for precision. The procedure was conducted aseptically. No adverse events or major complications were reported during PRP therapy except mild discomfort and pain at the injection site. It lasted only ten minutes and was relieved by its own [15]. However, the doctor prescribed Co-Codamol (30/500mg) to be taken twice daily if the pain persists.

However, after a week, the patient was affected by COVID-19 infection. Hence, he was administered the second final dose only after 21 days instead of 7 days. After 21 days, his PRP sample was not fit for administration due to difficulty processing the hemolysed sample.The final third dose of PRP was administered after 6 weeks post-COVID-19 infection.

Results

Before the COVID-19 infection, the platelet-rich plasma appeared to be clear. However, during the second final dose of PRP (21 days post-COVID-19 infection), the platelet-rich plasma appeared to be unclear despite performing centrifugation three times (Figures 1& 2), which returned to normal level after 6 weeks post-COVID-19 infection.

Figure 1: PRP extraction before COVID-19 infection.

Figure 2: PRP extraction afterCOVID-19 infection.

Parameters	**First PRP Injection (Before COVID-19)**	**Second PRP Injection (21 days after COVID-19)**	**Third PRP Injection (6 weeks after COVID-19)**
Platelet baseline	285 10^9/L	223 10^9/L	272 10^9/L
Platelet cell count	630 10^9/L	267 10^9/L	499 10^9/L
Haemoglobin	14.2	12.55	13.7
Normal haemoglobin range	13.0-17.0	13.0-17.1	13.0-17.2
RDW - SD	38.9	47.2	46.8
Normal RDW – SD range	35.1-43.9	35.1-43.10	35.1-43.11
RDW (CV)	12.7	14.55	15
Normal RDW (CV) range	11.6- 14.0	11.6- 14.1	11.6- 14.2

Table 1: Cell Count Analysis.

Table 1 highlights the comparative study of PRP levels before and after COVID-19 disease. The COVID-19

disease was associated with low haemoglobin saturation, elevated RDW level, and an increase in platelets level, which returned to normal levels after a few weeks.

Discussion

Since the patient was still experiencing COVID-19 symptoms, especially weakness, there was a change in plasma content. COVID-19 infectionis known to affect the lungs followed by walls thickening. As a result, there would be an increase in hematocrit values due to which plasma separation proved difficult, and PRP needed to be clarified. During the PRP extraction, various factors contribute to the platelet concentration gradient, such as the size of platelets, the biological difference among individuals, and hematocrit variability [16]. Some studies report that the hematocrit and total platelet count influence the platelet concentration of the PRP [17]. Blood with a low per cent hematocrit has more plasma available, diluting the platelet concentration in plasma [16]. Pan and colleagues observed a decrease in RDW and an increase in haemoglobin and hematocrit levels in COVID-19 patients [18].

Furthermore, non-severe and COVID-19 survivors have a higher platelet countthan severe and non-COVID-19 survivors. A thrombocytopenia condition in COVID-19 patients may be associated with a higher risk of death due to platelet consumption and coagulation abnormalities, including high fibrinogen and D-dimer levels. However, it was not the risk factor for mortality [19, 20].Similarly, a higher level of RDW was characterised by the overproduction of tumor necrosis factor and interleukins, followed by increased inflammation, elevated vascular permeability, and anticoagulant-procoagulant imbalance in patients with COVID-19 [21]. This was the first direct study that revealed the implication of COVID-19 infection on PRP extraction.

Study limitations

The current study's limitations include the need for follow-up, objective assessment of the interventional outcomes, and lack of a control group as it was a case study. Therehas been a lack of high-quality research studies on regenerative treatment for more than two years with multiple trial settings for knee osteoarthritis treatment.

Future investigations

The current observational study is in progress, thereby reporting the efficacy of PRP treatment on knee osteoarthritis post-COVID-19 infection in the following research paper.

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The participating patient had given his consent for the same. It is not a clinical trial; this was a study to check improvement in patient life after treatment was given; this treatment is already approved.

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Competing and Conflicting Interests

The authors declare that they have no competing interests.

Abbreviations

- KOA – Knee Osteoarthritis
- PRP - Platelet-Rich Plasma
- RDW - Red Blood Cell Distribution Width

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