EXERCISE INDUCED MUSCLE DAMAGE MAY BE IMPROVED BY A SINGLE DOSE OF INTRA-MUSCULAR PLATLET RICH PLASMA: A PILOT STUDY

Zekine Punduk,[1, A, D] Onur Oral,[2, A, D] Ramazan Aydinoglu,[2, B] Nadir Ozkayin[3, B]

[1] School of Physical Education and Sport, University of Balikesir, Balikesir, Turkey
[2] School of Physical Education and Sport, University of Ege, İzmir, Turkey
[3] Department of Orthopaedics and Traumatology Medical Faculty, University of Ege, Izmir, Turkey
[A] Study Design; [B] Data Collection; [C] Statistical Analysis; [D] Manuscript Preparation; [E] Funds Collection

Address for correspondence:
Zekine Punduk
Physical Education and Sports, University of Balikesir
PO 10050, Balikesir, Turkey
Phone: + 90 266 243 6447
Fax: + 90 266 239 0285
E-mail: zkn1938@gmail.com

Abstract. Platelet-rich plasma (PRP) is being increasingly used in the modern medicine as a material stimulating, regenerating and accelerating tissue healing, including muscle injuries in sports. The aim of the present study was to determine the effect of PRP on strength recovery in exercise induced muscle damage (EIMD). A baseline value was established in six healthy male volunteers during maximal voluntary strength isometric contractions (MVC) of the elbow flexors in both arms. This was followed by MVC performance (80% IRM) concentric-eccentric exercise of both elbow flexors until point of exhaustion, and 24 h later the subjects were injected with PRP in the non-dominant arm (PRP-arm). Maximal isometric strength and muscle soreness was compared before and at 24, 48, 72 and 96 h after delayed onset muscle soreness (DOMS) between the arms. The results indicate that the muscle soreness was significantly decreased in PRP administered arm when compared to control-arm, however, the levels for isometric flexors peak torque (PT) and average strength (AS) significantly declined in the bout arm post exercise induced muscle damage. Administration of PRP had no effect on the muscle strength parameters, however, flexor PT values were higher in PRP administered arm compared to the control arm, but this was only achieved on the second day of post-exercise induced muscle damage.

Key words: Platlet rich plasma, exercise induced muscle damage, muscle recovery, muscle soreness

Introduction

It is well established that physical exercise in the untrained individual can induce skeletal muscle damage (Kuipers 1994); this phenomenon is commonly known as “exercise-induced muscle damage” (EIMD) and is determined by the type, intensity and duration of exercise (Malm 2001) Symptoms of EIMD include reduced muscular force, increased stiffness, swelling, delayed onset muscle soreness (DOMS), and an increased release

of biomarkers related to muscle damage (Tee et al. 2007). In general, muscle soreness begins 24 h post exercise, peaks at between 48–72 h and persists for several days, hence it has been termed "delayed onset muscle soreness" (DOMS) (Clarkson and Sayers 1999) and it has been reported that during DOMS a decrease in the range of muscle motion and muscle force output can occur by up to 50% (Cleak and Eston 1992). Hence, DOMS can have a negative impact on the optimal performance of athletes due to exercise- induced muscle damage during training or competition.

Many studies have been published proposing various methods for treating DOMS, including cryotherapy, anti-inflammatory medication, stretching, hyperbaric oxygen, homeopathy, ultrasound, L-carnitine, rest, light exercise and electromagnetic shields (Cheung et al. 2003; Zhang et al. 2000; Almekinders 1999). For example, non-steroidal anti-inflammatory drugs (NSAIDs) are routinely prescribed to alleviate EIMD-related symptoms and restore normal physical function of the muscle. However, it has been reported that NSAIDs act by blocking COX and thus they may have a detrimental effect on muscle regeneration and super-compensation (Paulsen et al. 2010), and to date, an effective treatment for DOMS has not been established. Recently platelet-rich plasma (PRP), an autologous derivative of whole blood containing a supraphysiological concentration of platelets has gained increasing popularity in both the scientific literature and the wider media for its potential application in the treatment of traumatic musculoskeletal and sports-related injuries, cancer biology, and dermatology. In addition, it has been reported that PRP administration may improve recovery from tendon and muscle injuries (Gosens et al. 2011; Peerbooms et al. 2010). This has led the World Anti-Doping Agency (WADA) to question whether PRP should be classified as a doping agent due to the presence of growth factors. However, WADA has allowed the use of PRP since 2011 due to the lack of evidence supporting a systemic performance-enhancing effect and to allow further research to be conducted in this field. Only a few studies have addressed the systemic effects of locally administered PRP (Banfi et al. 2006; Wasterlain et al. 2013) however, these studies did not address the effect of PRP administration on athletic performance or muscle performance. To the best of our knowledge, no study has yet examined the effect of platelet-rich plasma (PRP) as a therapy for DOMS and specifically whether PRP can enhance muscle performance during this period. Therefore, we hypothesized that PRP therapy may decrease DOMS related symptoms and may play an important role in the regeneration of the muscle thus improving its performance. Hence, the purpose of this study was to determine the effect of PRP therapy on indicators of muscle pain and whether an increase in the recovery of muscle performance can be achieved post exercise-induced muscle damage.

Methods

Six moderately active male volunteers, mean age 27 ±3 years, weight 75.8 ±4.8 kg, and height 180.6 ±3.4 cm participated in this interventional pilot study. The subjects had not been involved in any regular weight-training program and had no history of injury to the arm, shoulder and elbow region. The nature and the risks of the experimental procedures were explained to the subjects, and signed informed consent to participate in the study was obtained. Before the test session, participants were examined and checked by the use of routine blood analysis by a medically qualified practioner. Ethical approval was obtained from The Balikesir University Medical Faculty Ethics Committee (2013/14) and each participant gave written informed consent prior to the study.

Performance test and muscle damage exercise protocol

In order to establish the baseline, the subjects performed the maximal voluntary strength of isometric contraction (MVC) (5 repetitions × 5 sec) of the elbow flexors in both the non-dominant and dominant arm at 90° elbow flexion by using a strain gauge device.

For the exercise-induced muscle damage test, subjects were seated on a bench with their arm positioned in front of their body and resting on a padded support, such that their shoulder was secured at a flexion angle of 0.79 rad (45°) and their forearm was maintained in the supinated position throughout the exercise. The elbow flexion and extension exercise was performed with 80% of MVC, 2-min rest between the sets until exhaustion was experienced. The subjects performed a mean average number of repetitions of (50 ±6) and a mean average number of sets (13 ±3) in order to induce muscle damage and the subjects were also given verbal encouragement by the investigator to maintain constant speed throughout the procedure. After the DOMS exercise, the subjects muscle strength performance was followed by the isometric test which was performed at the same time during the experimental period of four days. The isometric muscle performance is represented as a peak torque (PT, Nm) and the average strength as (AS, Nm).

Platelet-rich plasma

The participants non-dominant arms were treated post-24 h DOMS exercise with autologous PRP (Regen ACR-C, Regen Lab, Switzerland). Eight millilitres of peripheral blood was drawn from the dominant arm and the samples were centrifuged for 9 minutes at 3,500 revolutions per minute (H-19F, RegenCentrigel) according to manufacturers recommendation. Subsequently, 4 ml of PRP was injected using a 20-gauge needle into the region of the biceps brachii of the non-dominant arm under sterile aseptic conditions.

The muscle pain was evaluated according to the visual analogue scale data (VAS): 0- no pain, 10- the worst possible pain and muscle soreness was assessed on days 1–5 following the DOMS in the control and the PRP administered arm.

Statistical Analysis

All calculations were performed using SPSS software (SPSSInc, Chicago, Illinois, USA). Differences in continuous variables between arms were assessed using Student's t-test. Two-way repeated measures ANOVA with pairwise comparisons post hoc were applied to each data set to establish significant main effects. Data are expressed as means ±SE and the level of significance was set at $p < 0.05$.

Results

The baseline values for elbow flexors peak torque (PT) and average strength (AS) were similar between the control and the PRP administered arm ($p > 0.05$). In contrast, the isometric flexors PT values significantly declined in the control and the PRP admnistered on days 1–4 post exercise induced muscle damage (Figure 1). Similarly, the AS values also declined significantly in the control and PRP administered arm but this was only observed on days 1–2 post exercise induced muscle damage (Figure 2). There was no significant difference in the values for flexors PT and AS between the control arm and PRP administered arm between days 1–4 (Figures 1 and 2). Prior to the administration of PRP the flexors PT baseline value was 3% higher in the control arm when compared to the PRP

administered arm. However, post exercise-induced muscle damage the flexor PT value also increased by 3% in the PRP-administered arm when compared to the control arm but this was only observed on day 2, however, it did not reach statistical significance (Figure 1).

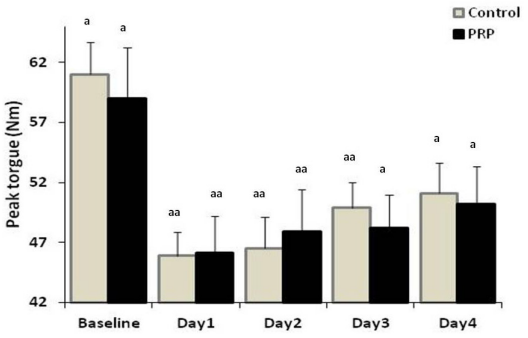

Figure 1. Maximum isometric peak torgue (PT) production of the elbow flexors at baseline and 1, 2, 3 and 4 day post exercise induced muscle damage. Significant reduction from baseline $^{a}P < 0.05$, $^{aa}P < 0.01$. Data are presented as means ± SE. Abbreviations: Control, (Control arm); PRP, platelet rich plasma administered arm. No significant differences were observed between control and PRP administered arm in experimental sessions $P > 0.05$.

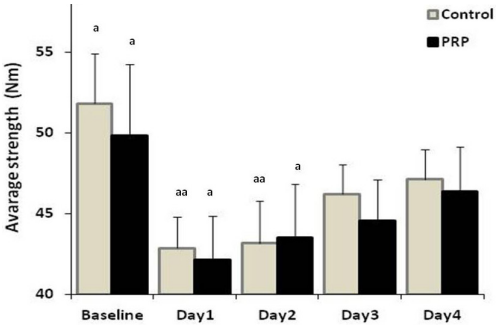

Figure 2. Average isometric strength of the elbow flexors at baseline and 1, 2, 3 and 4 day post exercise induced muscle damage. Significant reduction from baseline $^{a}P < 0.05$, $^{aa}P < 0.01$. Data are presented as means ± SE. Abbreviations: Control, (Control arm); PRP, platelet rich plasma administered arm. No significant differences between control and PRP arm were observed in experimental sessions $P > 0.05$.

There was also no significant difference in the muscle strength loss values post exercise- induced muscle damage between the control arm and the PRP administered arm between days 1–4 ($p > 0.05$) (Figure 3). However, the elbow flexor strength loss was 12% and 22% less on days one and two respectively in the PRP administered arm when compared to the control arm (Figure 3).

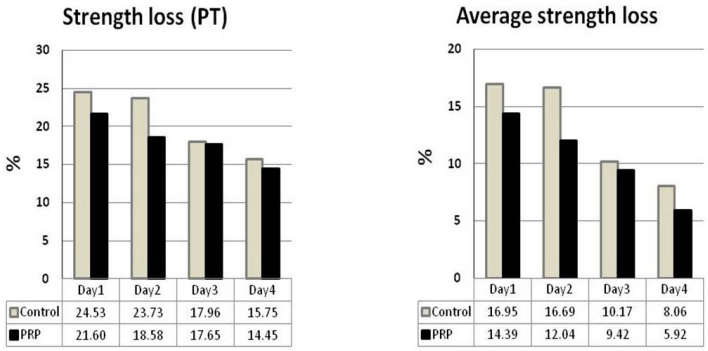

Figure 3. Isometric strength loss of the elbow flexors at baseline and 1, 2, 3 and 4 day post exercise induced muscle damage. Data are presented as means ± SE. Abbreviations: Control, (Control arm); PRP, platelet rich plasma administered arm. No significant differences between control and PRP administered arm were observed in experimental sessions P > 0.05.

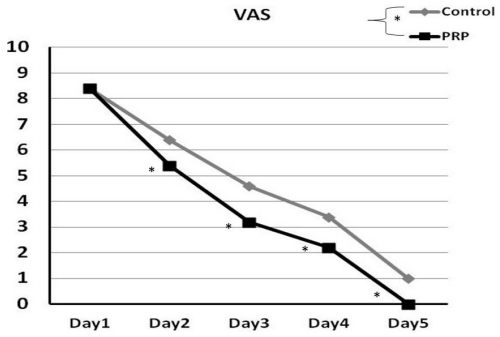

Figure 4. Average VAS of perceived muscle soreness 1, 2, 3 and 4 day post exercise induced muscle damage. Muscle soreness scored was significantly decreased in PRP arm *P < 0.05. Data are presented as means ± SE. Abbreviations: Control, (Control arm); PRP, platelet rich plasma injected arm.

The VAS scores were also estimated between days 1–5 post excercise-induced muscle damage in the control arm and PRP administered arm and are presented in Figure 4. The VAS scores peaked on day 1 for the control arm and the PRP administered arm, however, no statistical sinificance was observed between them (P > 0.05). In contrast, the control arm displayed significantly higher VAS scores and hence greater muscle soreness compared to the PRP administered arm between days 2–5 (P = 0.02, P = 0.05, P = 0.02, P = 0.01) respectively.

Discussion

Many methods have been utilised for the treatment of DOMS, including cryotherapy, anti-inflammatory medication, stretching, hyperbaric oxygen, homeopathy, ultrasound, L-carnitine, rest, light exercise and electromagnetic shields (Cheung et al. 2003; Zhang et al. 2000; Almekinders 1999). Inflammatory conditions have

been essentially treated by the use of non-steroidal anti-inflammatory drugs (NSAIDs) although they are ineffective in reducing muscle pain and do not increase muscle performance during DOMS (Paulsen et al. 2010; Semark et al. 1999; Kuipers et al. 1985; Bourgeois et al. 1999). As an alternative to conventional treatments, platelet-rich therapy has been applied due to its potential in accelerating muscle healing and reducing a player's injury time. As far as we are aware, this study is the first to examine the effect of intramuscular PRP administration on DOMS and muscle strength post exercise-induced muscle damage during the recovery period in healthy human volunteers. Our results show that elbow flexors muscle strength PT values were improved approximately by 3% after PRP administration when compared to the control arm, this was achieved on the second day of DOMS period post exercise-induced muscle damage. Furthermore, percentile strength loss was lower on day 1 compared to day 2 (12% vs 22%) in the PRP administered arm when compared to the control arm following exercise-induced muscle damage. These results are novel and to the best of our knowledge, no data exists concerning the acute effect of PRP administration on muscle strength parameters during recovery period in an exercise-induced muscle damage model.

In general, related studies have investigated the effect of the PRP administration on muscle injuries in sports. Several studies have suggested that PRP may be advantageous in sports medicine, but up until now, the majority of human studies supporting this hypothesis are either small case series, or level 4 and 5 studies, demonstrating the efficacy of PRP on muscle regeneration. For instances, PRP has been suggested as a potential intervention agent in the treatment of acute muscular injuries (Lopez-Vidriero et al. 2010), improvement of grade-2 hamstring injuries (Hamid et al. 2012), and enhancement of physical recovery and regeneration compared with conventional conservative treatments in acute muscle trauma in professional athletes (Bubnov et al. 2013). Accordingly, administration of PRP results in significant changes in the strength and range of motion in acute muscle injury between days 7 and 14 (Bubnov et al. 2013). Virchenko and Aspenberg (2006) have reported that administration of PRP in combination with stretching and strengthening exercises plays a key role in the treatment of tendon injury. In support of this, Gobbi and Bathan (2009) study demonstrated that PRP combined with optimum nutrition, exercise, and lifestyle can act as a preventive agent in chronic and degenerative musculoskeletal disease. Although the prohibition of intramuscular injections of PRP has been removed from the 2011 Prohibited List, WADA continues to review the use of PRP as and when new medical and scientific information becomes available (Engebretsen et al. 2010). Currently there is a lack of evidence concerning the use of PRP for performance enhancement beyond its potential therapeutic effect (WADA).

Athletes commonly return to training 48 h following competition, hence fast muscle recovery is important during this time (Jakeman et al. 2010). The ability to train consistently at high levels is important for athletes, and the potential advantage offered by PRP for muscle strength recovery post exercise-induced muscle damage should be considered. We observed that muscle soreness decreased markedly in the PRP administered arm during the DOMS period. Most of the studies have shown that administration of PRP significantly improves outcome scores, including VAS (commonly used measures of pain intensity) and DASH (disabilities of the ARM, Shoulder, and Hand) scores in the experimental groups compared to the control groups, which were injected with either whole blood, saline, or corticosteroids (Peerbooms et al. 2010; Hechtman et al. 2011; Thanasas et al. 2011). Indeed, the demonstrated modulation of the inflammatory response may explain the pain reduction usually observed after PRP administration and may account for the early mobilization of treated patients. It has also been reported that 24 hours post PRP administration systemic levels of some growth factors such as vascular endothelial growth factor and

epidermal growth factor are modified (Banfi et al. 2006; Wasterlain et al. 2013). This may have a favorable effect on muscle strength recovery during the DOMS period.

Our results are novel and suggest that intramuscular administration of PRP may improve muscle strength recovery and also, it may have a role to play in accelerating exercise induced muscle damage recovery. However, further studies are needed to validate this work especially with regards to doping regulations.

Practical applications

Many methods have been used for the treatment of DOMS. Generally, inflammatory conditions have been essentially treated by the use of non-steroidal anti-inflammatory drugs (NSAIDs) although they are ineffective in reducing muscle pain and do not increase muscle performance during DOMS. PRP may improve the training adaptation cycle by speeding-up the recovery of the muscle strength and pain level of the overreach symptoms in the athletes.

Acknowledgements

The authors would like to thank the volunteers who took part in this study.

References

Almekinders L.C. Anti-inflammatory treatment of muscular injuries in sport. An update of recent studies. Sports Med. 1999; 28 (6): 383–388.

Banfi G., Corsi M.M., Volpi P. Could platelet rich plasma have effects on systemic circulating growth factors and cytokine release in orthopaedic applications? Br J Sports Med. 2006; 40 (10): 816.

Bourgeois J., MacDougall D., MacDonald J.A.Y., Tarnopolsky M. Naproxen does not alter indices of muscle damage in resistance-exercise trained men. Med Sci Sports Exerc. 1999; 31 (1): 4–9.

Bubnov R., Viacheslav Y., Semeniv I. Ultrasound guided injections of Platelets Rich Plasma for muscle injury in professional athletes. Comparative study. Med Ultrason. 2013;.15.(2):.101–105.

Cheung K.H., Patria A., Maxwell L. Delayed onset muscle soreness: treatment strategies and performance factors. Sports Med. 2003; 33 (2): 145–164.

Clarkson P.M., Sayers S.P. Etiology of exercise-induced Muscle damage. Can J Appl Physiol. 1999; 24: 234–248.

Cleak M., Eston R. Muscle soreness, swelling, stiffness and strength loss after intense eccentric exercise. Br J Sports Med. 1992; 26: 267–272.

Engebretsen L., Steffen K., Alsousou J., Anitua E., Bachl N., Devilee R., Everts P., Hamilton B., Huard J., Jenoure P., Kelberine F., Kon E., Maffuli N., Matheson G., Mei-Dan O., Menetrey J., Philippon M., Randelli P., Schamasch P., Schwellnus M., Vernec A., Verrall G.. IOC consensus paper on the use of plateletrich plasma in sports medicine. Br J Sports Med. 2010; 44: 1072–1081.

Gobbi A., Bathan L. Biological approches for cartilage repair. J Knee Surg. 2009; 22 (1): 36–44.

Gosens T. Peerbooms J.C., van Laar W., den Oudsten B.L. Ongoing positive effect of platelet-rich plasma versus corticosteroid injection in lateral epicondylitis: a double-blind randomized controlled trial with 2-year follow-up. Am J Sports Med. 2011; 39 (6): 1200–1208.

Hamid M.S.A., Ali M.R.M., Yusof A., George A. Platelet-rich plasma (PRP): an adjuvant to hasten hamstring muscle recovery. A randomized controlled trial protocol (ISCRTN66528592). BMC Musculoskelet Disord. 2012; 13: 2–8.

Hechtman K.S., Uribe J.W., Botto-vanDemden A., Kiebzak G.M. Platelet-rich plasma injection reduces pain in patients with recalcitrant epicondylitis. Orthopedics. 2011; 34: 92.

Jakeman J.R., Byrne C., Eston R.G. Lower limb compression garment improves recovery from exercise-induced muscle damage in young, active females. Eur J Appl Physiol. 2010; 109 (6): 1137–1144.

Kuipers H., Keizer H.A., Verstappen F.T., Costill D.L. Influence of a prostaglandin-inhibiting drug on muscle soreness after eccentric work. Int J Sports Med. 1985; 6 (6): 336–339.

Kuipers H. Exercise-induced muscle damage. Int J of Sports Med. 1994; 15: 132–135.

Lopez-Vidriero E., Goulding K.A., Simon D.A., Sanchez M., Johnson D.H. The use of platelet-rich plasma in arthroscopy and sports medicine: optimizing the healing environment. Arthroscopy. 2010; 26 (2): 269–278.

Malm C. Exercise-induced muscle damage and inflammation: Fact or fiction? Acta Physiol Scand. 2001; 171: 233–239.

Paulsen G., Egner I.M., Drange M., Langberg H., Benestad H.B., Fjeld J.G., Hallen J., Raastad T. A COX-2 inhibitor reduces muscle soreness, but does not influence recovery and adaptation after eccentric exercise. Scand J Med Sci Sports. 2010; 20 (1): 195–207.

Peerbooms J.C., Sluimer J., Bruijn D.J., Gosens T. Positive effect of an autologous platelet concentrate in lateral epicondylitis in a double-blind randomized controlled trial: platelet-rich plasma versus corticosteroid injection with a 1year follow-up. Am J Sports Med. 2010; 38: 255–262.

Semark A., Noakes T.D., Gibson A.S.C., Lambert M.I. The effect of a prophylactic dose of flurbiprofen on muscle soreness and sprinting performance in trained subjects. J Sports Sci. 1999; 17 (3): 197–203.

Tee J.C., Bosch A.N., Lambert M.I. Metabolic consequences of exercise-induced muscle damage. Sports Med. 2007; 37: 827–836.

Thanasas C., Papadimitriou G., Charalambidis C., Paraskevopoulos I., Papanikolaou A. Platelet-rich plasma versus autologous whole blood for the treatment of chronic lateral elbow epicondylitis: a randomized controlled clinical trial. Am J Sports Med. 2011; 39: 2130–2134.

Virchenko O., Aspenberg P. How can one platelet injection after tendon injury lead to a stronger tendon after 4 weeks? Interplay between early regeneration and mechanical stimulation. Acta Orthop. 2006; 77 (5): 806–812.

Wasterlain A.S., Braun H.J., Harris A.H., Kim H.J., Dragoo J.L. The systemic effects of platelet-rich plasma injection. Am J Sports Med. 2013; 41 (1): 186–193.

Zhang J., Clement D., Taunton J. The efficacy of Farabloc, an electromagnetic shield, inattenuating delayed-onset muscle soreness. Clin J Sport Med. 2000; 10 (1): 15–21.

Cite this article as: Punduk Z., Oral O., Aydinoglu R., Ozkayin N. Exercise induced muscle damage may be improved by a single dose of intra-muscular platlet rich plasma: A Pilot Study. Centr Eur J Sport Sci Med. 2014; 8 (4): 19–26.