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Platelet-Rich Plasma in the Treatment of "Frozen Shoulder"

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ABSTRACT

Introduction: This paper presents the results of treating the condition known as frozen shoulder with the platelet-rich plasma method (PRP). Frozen shoulder (periarthritis humeroscapularis, adhesive capsulitis) is the third most common condition (after back pain and knee arthrosis) occurring in middle-aged people (40 to 60 people).

Aim of the Study: To establish to which extent is platelet-rich plasma efficient in the treatment of painful shoulder syndrome.

Patients and Methods: In the period between January 2013 and December 2015, in the HI Hospital for Surgical and Internal Medicine "S.tetik", 54 female patients with clinical manifestations of a frozen shoulder were treated. The treatment consisted of three PRP administrations at 7-day intervals. The Quick Dash questionnaire was used for the results at the beginning of the treatment, as well as 30 days and 3 months after its completion. A checkup was conducted after a year.

Results: In total, we treated 54 female patients whose average age was 52 years (37 – 72). Pain in the left shoulder was experienced by 37 patients, while 17 of them experienced pain in the right shoulder. The Quick Dash score prior to the PRP administration was 42 (35-52), while after the PRP treatment the score was 18 (13-26) after 30 days and 13 (11-23) after 3 months.

Conclusion: By means of our protocol, implying the treatment of frozen shoulder with the platelet rich plasma method, it is possible to significantly reduce subjective difficulties of patients. Also, together with all other therapeutic procedures (analgesia, physical therapy, etc.), it may eventually lead to a complete recovery. Further work on the examination of pathophysiological effects of PRP and monitoring a large number of patients in multiple centers could result in scientifically proven standards for the application of PRP as a method of choice in the treatment of frozen shoulder.

Key words: Platelet-rich plasma, frozen shoulder, Quick Dash score

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Introduction

Frozen shoulder is a syndrome characterized by pain and limited active movements in the shoulder joint. The etiology of the condition itself has not been precisely defined yet. It is most common in the population aged between 40 and 65, occurring much more frequently in women (4:1).[1] In Japan, it is known as "50s shoulder". The term "frozen shoulder" was first described by Codman in 1934. He regarded this condition as a painful condition associated with shoulder stiffness and pain when sleeping on the affected shoulder. He also described the phenomenon of limitation of external rotation and elevation, which are standard diagnostic criteria still used to this day. Long before Codman, in 1845, Duplay named this condition periarthritis, while in 1872, Naviesar coined the term adhesive capsulitis. Pain in the shoulder joint is the third most common cause of disability, after lower-back pain and pain in the knee. The incidence of frozen shoulder in the total population is 2% and up to 11% in diabetics, occurring on both sides in 16% of patients.[1] The disease has been described as passing through three stages and each of these is specific and characteristic in terms of symptoms indicated by the patient. Stage 1 – painful phase – the patient describes an insidious onset of pain, with the pain usually occurring at night, without causal factors. The pain is not associated with activity, even though the slightest movement can increase it. As the disease progresses, patients feel pain even at rest. In this stage, which can last anywhere between 2 and 9 months, there is no loss of range of motion, while clinical presentation may be diagnostically unclear. Stage 2 – frozen phase – painful symptoms from the stage 1 may still be present, but they are most often improved. The loss of range of motion occurs as capsular pain (in all directions of movement). Daily activities may be rather affected. This stage of the disease may last between 2 and 9 months, and even up to 24 months. Stage 3 – thawing phase or regression phase – the pain begins to fade gradually and shoulder motion is slowly improved in the next 12 to 24 months.

The diagnosis is established based on a medical history and clinical examination, as well as standard X-ray imaging and possibly CT and MR. In the differential diagnosis, the diseases which should be taken into account are rupture and tendinitis of the two-headed muscle of the upper arm (m. biceps brachii), brachial plexus neuritis, cervical spine disorders (arthrosis, bulging or prolapsed cervical disc, torticollis), Parkinson's disease and primary and secondary tumors, Pancoast lung tumor in particular. The treatment involves rest, non-steroidal anti-inflammatory drugs, physical therapy, intra-articular administration of corticosteroids and arthroscopic procedures. In addition to the above mentioned treatment methods, a relatively new method used to treat bone and joint diseases is the platelet-rich plasma – PRP method. The first serious attempts at treatment by this method were described in the 70s of the last century and the first works dealing with this subject were published at the beginning of the 21st century, for soft tissue injuries and healing of skin defects, treatment of knee injuries after arthroscopic surgery (Sánchez et al. 2003), for muscle injuries (Sánchez et al. 2005), for tendon treatment (Sánchez et al. 2007), for knee arthrosis (Sánchez et al. 2008) and hip arthrosis (Sánchez et al. 2011).[3] PRP works through growth factors which play a key role in initiating and controlling the complex process of rehabilitation of injuries and diseases. This treatment method relies on an increased concentration of platelets which contain high concentrations of growth factors. Growth factors stimulate repair and healing of tendons, ligaments and cartilage, epithelialization and formation of new connective tissue. It is highly important that growth factors are derived from the patient's own blood, in order to avoid an autoimmune reaction of the organism during their administration.[4] Growth factors involved in PRP are: PDGF - *platelet-derived growth factor*, TGFB - *transforming growth factor beta*, FGF - *fibroblast growth factor*, ILGF 1 - *insulin-like growth factor 1*, ILGF 2 - *insulin-like growth factor 2*, VEFR - *vascular endothelial growth factor*, EGF - *epidermal growth factor, interleukin 8*, CGF - *Keratinocyte growth factor*, and CTGF - *connective tissue growth factor*. Worldwide, there are dozens of commercial systems for the preparation of plasma in which platelet count is 2 to 10 times higher compared with whole blood. Based on the results achieved in terms of platelet count, PRP is categorized.[5,6] Some of the systems used to categorize PRP are:

1. PAW (platelets, activators, white blood cells) provides an absolute white blood cell count and platelet count, as well as information about whether activators are used or not.

2. Mishra and Pavelko, together with colleagues from Stanford University in the United States of America, published the first-in-human study on the use of PRP in 2006 and they categorized PRP according to platelet count, white blood cell count, and presence or absence of PRP activators (Table 1).[7]

Table 1. Mishra et al. PRP classification

Type	Platelet concentration	White blood cell count	Activator
1	A) 5 or more times higher compared with whole blood B) up to 5 times higher compared with whole blood	increased	Without an activator
2	A) 5 or more times higher compared with whole blood B) up to 5 times higher compared with whole blood	increased	With an activator
3	A) 5 or more times higher compared with whole blood B) up to 5 times higher compared with whole blood	Minimal or without white blood cells	Without an activator
4	A) 5 or more times higher compared with whole blood B) up to 5 times higher compared with whole blood	Minimal or without white blood cells	With an activator

Aim of the Study

To establish to which extent is platelet-rich plasma efficient in the treatment of painful shoulder syndrome.

Patients and Methods

In the period between January 1st,2013 and December 31st, 2015 we treated 54 female patients with clinical manifestations of a frozen shoulder. All the patients experienced pain in one shoulder only. Pain lasted for three or more months and standard treatment procedures had been previously applied, including the use of analgesics, physical therapy and the administration of at least two doses of corticosteroids to the painful shoulder. The diagnosis was established on the basis of clinical presentation and X-ray imaging. Before the treatment was initiated, the patients filled in the Quick Dash score (The Disabilities of the Arm, Shoulder and Hand Score), which consisted of 11 questions about daily activities, providing 5 possible answers (no difficulties, slightly impaired function and pain, moderate pain and impaired functions, severe pain and all functions significantly impaired, and constant pain without any movement) (Table 2).[8]

Table 2. Quick DASH Score

Function	No difficulty	Mild	Moderate	Severe	Extreme
Opening a jar	1	2	3	4	5
Doing heavy household chores (washing walls and floors)	1	2	3	4	5
Carrying a shopping bag	1	2	3	4	5
Washing your back	1	2	3	4	5
Using a knife to cut food	1	2	3	4	5
Recreational activities or repeated use of the arm	1	2	3	4	5
Difficulties with prolonged sitting or moving, not using the arm, during the past week	1	2	3	4	5
Limitations in the work during the past week	1	2	3	4	5
Shoulder pain	1	2	3	4	5
Tingling, unpleasant feeling in the shoulder	1	2	3	4	5
Pain during sleep	1	2	3	4	5

The protocol of platelet-rich plasma administration was unique and the administration was carried out three times at 7-day intervals. Blood was prepared and PRP was administered in the morning. We collected 10 to 40 ml of blood from the patients; the blood was treated without an anticoagulant in a centrifuge, at a speed between 600 and 3,000 rpm, for 6 to 10 minutes. Upon the preparation of an area for administration using a preparation of iodine, the administration was done using a hypodermic needle to the subacromial bursa with aspiration and the application of PRP. Local anesthetics were not given. Following the administration, puncture site was covered with sterile gauze which was removed after one hour. The results were monitored with the *Quick Dash*, whose outcome was categorized as follows: no difficulty (up to 11 points), mild difficulty (12 to 22 points), moderate difficulty (23 to 33 points), severe difficulty (34 to 44 points), and extreme difficulty (45 to 55 points) (Table 3).

Table 3. Valorization of the Quick DASH score

	Quick Dash Score	Difficulty level	Function
1	11	No difficulty	Excellent
2	12-22	Mild difficulty	Good
3	23-33	Moderate difficulty	Satisfactory
4	34-44	Severe difficulty	Poor
5	45-55	Extreme difficulty	Unable to move

DASH:Disabilities of Arm, Shoulder and Hand

Results

In total, we treated 54 female patients whose average age was 52 years (37 – 72). Pain in the left shoulder was experienced by 37 patients (68%), while 17 of them (32%) experienced pain in the right shoulder. The mean amount of blood collected from the patients was 21.8 ml (10 – 40). The amount of produced PRP was 3.1 ml (1.7 to 4.9) using 10 ml of whole blood, with a mean value of platelets in whole blood of 198,000 ml (131 to 259), and of 708,000 platelets per ml (314 to 943) in the platelet-rich plasma. White blood cell count in whole blood amounted to 6.2 (3.1 to 8.7) on the average, while in the platelet-rich plasma it amounted to 11.3 (7.3 to 14.9). According to the Mishra et al. classification, our produced PRP belonged to the 1B group. The Quick Dash score prior to the PRP administration was 42 (35-52), while after the PRP treatment, the score was 18 (13-26) after 30 days and 13 (11-23) after 3 months. From a total of 54 female patients, after three months of the PRP treatment, 48 (89%) experienced no difficulties which would require further treatment, in 3 patients (5.5%), the PRP treatment was repeated after three months and their state was good afterwards, while 3 patients (5.5%) were treated by administering corticosteroids three months after PRP and upon physical treatment their state was orderly, without difficulties. A year after the PRP treatment, none of the 51 patients who were monitored experienced a recurrence of the disease.

Discussion

Treatment of a condition known as "frozen shoulder" represents a challenge faced by a team of orthopaedists and physiatrists. Taking into consideration that this condition affects working-age population, a successful recovery is even more important. Since standard methods applied by orthopaedists and physiatrists sometimes do not achieve satisfactory results, the platelet-rich plasma treatment appears to be a possible solution.[9,10] In a study by Aslani et al. entitled "Platelet-Rich Plasma for Frozen Shoulder: A Case Report", published in Arch Bone Jt Surg. in 2016, 70% improvement for function was reported after the treatment using PRP.[11] Our paper demonstrates that the treatment of "frozen shoulder" using the platelet-rich plasma method results in a subjective and objective improvement immediately after the drug administration, and particularly after three months. Obviously, this treatment method should be accompanied with all other standard treatment methods applied by orthopaedists and physiatrists.

Conclusion

In order to confirm the success of the treatment with this method, it is necessary to carry out extensive multicentre trials and to set standards in terms of the number of administrations, the frequency of administration, the number of platelets, with or without white blood cells, etc. Given the fact that this is a relatively painless method, with a small number of possible complications and good initial results, this method is becoming an indispensable part of the treatment for "frozen shoulder".

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Plazma obogaćena trombocitima u liječenju "zamrznutog ramena"

SAŽETAK

Uvod: U radu su prikazani rezultati liječenja oboljenja ramena poznatog kao zamrznuto rame metodom plazme obogaćene trombocitima(PRP)."Zamrznuto rame"(frozen shoulder, periarthritis humeroscapularis, adhezivni kapsulitis) je treće (nakon bolnih leđa i artroza koljena) najčešće oboljenje koje se javlja kod osoba srednje životne dobi (40-60 godina).

Cilj rada: Utvrditi koliki efekat liječenja bolnog sindroma ramena ima plazma obogaćena trombocitima.

Ispitanici i metode: U Bolnici "S.tetik" Banja luka, u periodu od januara 2013. do decembra 2015., liječili smo ukupno 54 osobe ženskog pola sa kliničkim manifestacijama "zamrznutog ramena". Tretman se sastojao od 3 aplikacije PRP u razmaku od po 7 dana. Za rezultate smo koristili Quick Dash upitnik na početku liječenja te 30 dana i 3 mjeseca po završenom liječenju. Kontrolni pregled smo radili nakon godinu dana.

Rezultati: Ukupno smo liječili 54 osobe ženskog pola, prosječne starosti 52 godine (37-72). Kod 37 pacijentkinja bolno je bilo lijevo rame, a kod 17 desno rame. Vrijednost Quick Dash scora prije započinjanja terapije PRP je bila 42 (35-52). 30 dana nakon primjene tretmana PRP, vrijednost je bila 20 (13-26), dok je nakon 3 mjeseca primjene tretmana vrijednost bila 18 (11 – 23).

Zaključak: Primjenom našeg protokola liječenja "zamrznutog ramena" metodom plazme obogaćene trombocitima, subjektivne tegobe oboljelih je moguće značajno smanjiti te uz primjenu svih ostalih terapijskih procedura (analgezija,fizikalna terapija...) dovesti do potpunog izlječenja. Daljim radom na ispitivanju patofiziološkog djelovanja PRP te praćenjem većeg broja oboljelih u više centara mogli bismo postići naučno dokazane standarde za primjenu PRP kao metode izbora u liječenju "zamrznutog ramena".

Ključne riječi: Plazma obogaćena trombocitima, zamrznuto rame, Quick Dash score