Journal of Back and Musculoskeletal Rehabilitation -1 (2019) 1–10 DOI 10.3233/BMR-191519 IOS Press

Comparison of ultrasound-guided platelet rich plasma, prolotherapy, and corticosteroid injections in rotator cuff lesions

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Abstract.

BACKGROUND: Injections is a good alternative to conventional treatment-resistant cases with rotator cuff (RC) lesions before operation. Currently, different injection methods are used in RC lesions.

OBJECTIVE: To evaluate the efficacy of different injection methods (pre-ext-rich plasma [PRP], corticosteroid [COR] and prolotherapy [PRO]) in RC tendon lesions.

METHODS: One hundred and twenty-nine patients were divided in to groups as PRP, COR, PRO and the lidocaine group. Subacromial injection was applied to all groups. They were evaluated using the Visual Analogue Scale (VAS), American Shoulder and Elbow Surgeons Standardized Shoulder Assessment Form (ASES), and Western Ontario Rotator Cuff Index (WORC) at 3, 12 and 24 weeks post-injection.

RESULTS: In the COR group in the 3rd week, VAS and WOLC scores were significantly lower than the other groups (p < 0.01 and p < 0.05 respectively). In the PRP group in the 14th week, VAS and WORC scores were found to be significantly lower than the COR group (p < 0.01 and p < 0.05 respectively). In the COR group in the 3rd week the ASES score was found to be significantly higher than the PRP and PRO group (p < 0.01).

CONCLUSION: In patients with RC lesicns, corticosteroid injection provides short-term relief for pain, function, and quality of life, while PRP injection works for lor 2-term wellbeing. For all types of applied injections, improvement in pain, function and quality of life were observed.

Keywords: Injection, rotator cyff wolon, prolotherapy, platelet-rich plasma, corticosteroid, randomized clinical trial

1. Introduction

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Rotator cuff (RC) tendon problems can be seen in one out of every five people [1]. The lesions are evaluated and diagnosed by sports physicians, physiatrists, and orthopedists, with different clinical pictures rang-

6 ing from acute tendinitis to full-thickness tears. In-

ternal and external factors, such as age-related de-7 generation, anatomical differences, and biomechanical problems, prepare the ground for the development of RC tendinopathy. The mechanism and pathogenesis of 10 tendinopathy differ between age groups. In younger 11 subjects, it is caused by recurrent overuse injuries or 12 acute traumatic events, but at later ages, it develops 13 in association with age-related degeneration without 14 trauma. Education, rest, activity modification, ice ap-15 plication, physical therapy applications, exercise, and 16 nonsteroidal anti-inflammatory drugs (NSAIDS) are 17 the non-surgical approach to treating these problems. 18 Subacromial injection is another treatment approach if 19

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healing is not achieved with these applications. Sub-20 acromial corticosteroid injection is an injection method 21 that has been implemented for a short-term basis for 22 many years [2,3]. Due to the limited capacity of the 23 tendons to self-repair [4], new biological treatment 24 methods have been brought into the agenda for the 25 treatment of tendinopathies in recent years. However, 26 there is not enough scientific evidence about their ef-27 fectiveness. 28

Although the mechanism of prolotherapy is not 29 clear, increased glucose in the extracellular matrix is 30 thought to stimulate healing and tissue regeneration 31 by eliciting an acute inflammatory response, fibroblast 32 proliferation, and subsequent collagen synthesis [5]. 33 According to another theory, high concentrations of 34 dextrose cause osmotic rupture of local cells [6]. In-35 creasing glucose in the extracellular matrix induces 36 an acute inflammatory response and stimulates fibrob-37 last proliferation. Then, new collagen synthesis is initi-38 ated [5]. PRP is an autologous blood product in which 39 a person's blood is included in the tissue healing pro-40 cess of supraphysiological platelets, and growth fac-41 tors are released from the platelets [7,8]. These growth 42 factors are transforming growth factor beta (TGF- β), 43 platelet-derived growth factor (PDGF), vascular en-44 dothelial growth factor (VEGF), hepatocyte growth 45 factor, and insulin-like growth factor 1 (IGF-1) [9]. An-46 though these factors are biologically active, they pro-47 duce angiogenesis, epithelization, cell differentiation, 48 proliferation of the extracellular matrix, and fil rovas-49 cular callus [10,11]. The aim of our stud over s to com-50 pare the effectiveness of different injection methods 51 with corticosteroids, PRP, and prototherapy in compar-52 ison with lidocaine in treatment-resistant rotator ten-53 don lesions. 54

55 2. Methods

The study was planned as a randomized controlled 56 trial in patients with RC lesions from sports medicine 57 and physical therapy and rehabilitation outpatient clin-58 ics. Ethics committee approval was granted for the 59 study, and a signed informed consent form was ob-60 tained from each patient. A total of 232 partici-61 pants with symptoms of RC tendon injury were eval-62 uated between June 2014 and January 2018. The 63 participants were randomly assigned by a computer-64 generated program as the PRO, PRP, COR, and lido-65 caine groups. Each patient was evaluated before injec-66 tion, and planned injections were applied. Only one 67

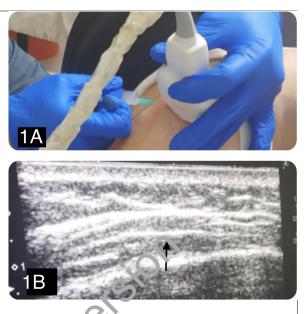
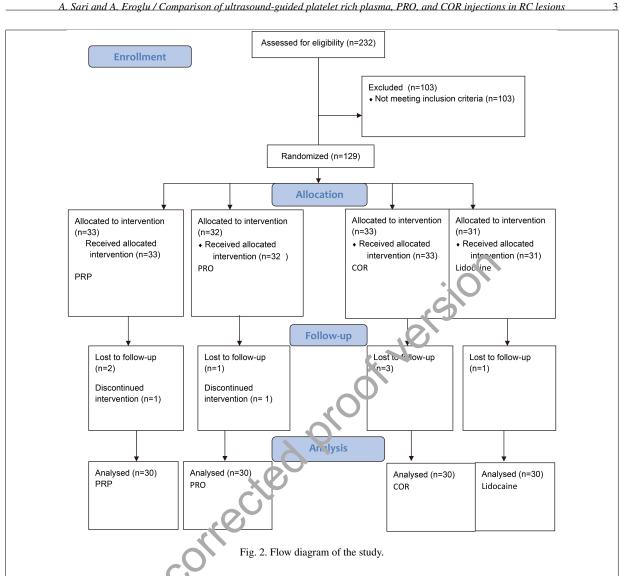


Fig. 1. A: Ultra o ...d- uided subacromial postero-lateral injection. B: Ultrasound in the of an in-plane lateral to-medial approach of a 21 gauge meedle (arrow) placement.

injection was applied to each person in each group. 68 In practice, the lateral subacromial injection method 69 was preferred. For a safer and more efficient injec-70 tion application, all applications were performed with 71 USG (Toshiba Aplio 300 Japan 7.5 Hz linear probe) on 72 the sagittal axis with the long axis in-plane technique. 73 From a technical perspective, the patient sits in an up-74 right position with the arms behind the back, internal 75 rotation, shoulder in hyperextension, and elbow 90° 76 degrees parallel to the ground for a subacromial view 77 (Fig. 1). The USG in-plane technique was used in the 78 subacromial area to confirm that the needle remained 79 in the correct location as it progressed. The same tech-80 nique was used for all patients. The needle endpoint 81 was subacromial bursae. The nurse, preparing the in-82 jection solution, covered each injector syringe with an 83 invisible opaque tape. The physician who applied the 84 injection to the patient, the patient, and the physician 85 who evaluated the patient after the injection did not 86 know which injection had been applied to the patient. 87 The information contained in the relevant nurse docu-88 mentation and data from the chart were combined by 89 the relevant data specialist, and the study data were 90 created. The participants underwent face-to-face eval-91 uations at the clinic at 3 and 12 weeks after injection 92 and by phone after 24 weeks. The standard shoulder 93 strengthening and stretching exercise programs were 94 given to each group for 6 weeks. After the injection, 95 the participants were told not to take any pain medi-96



cation other than paracetamel. Padients were included 97 in the study if they met the following criteria: they 98 were aged 18-75 years; had experienced shoulder pain 99 for at least 3 months; had RC pathology (bursitis, RC 100 tendinosis, or partial tears grade I) treated with non-101 invasive treatments, including NSAIDs and/or at least 102 2 months of regular exercise and/or physical therapy 103 agents (TENS, ultrasound, etc.); and their condition 104 had been evaluated via clinical and physical exami-105 nation and confirmed with recent magnetic resonance 106 imaging (MRI). Exclusion criteria are; RC total or >107 grade 1 partial rupture, treatment with NSAID within 108 the last week, allergic reactions to disinfectants, lo-109 cal anesthetics, sodium citrate and calcium chloride, 110 thrombocytopenia, acute and chronic infections, anti-111 coagulation or anti-aggregation therapy, any previous 112 shoulder injection, glaucoma, hypertension, systemic 113

allergy or hypersensitivity, severe renal or hepatic insufficiency, within 6-12 weeks of surgery at the treatment site, malignancy, pregnancy, uncontrolled diabetes, prosthetic joint, age < 18 y/o, significant skin breakdown at the proposed injection site, the presence of a joint prosthesis, joint instability, adjacent superficial skin lesions or abrasions, severe osteoporosis of bones adjacent to the joint or if the patient is unable to provide informed consent.

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Among 232 volunteers, 129 met the eligibility criteria and were included in the study. During the study period, 9 people were excluded from the study due to reasons such as refusal of treatment and failure to adapt to the study. The flow diagram of the study is shown in Fig. 2. All injections were done with sterile 5 mL solutions using a 21 G 38 mm needle. The PRO group was given 5 mL of prolotherapy solution (a mixture of 4 mL

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20% dextrose and 1 mL lidocaine); the COR group was 131 given 2 mL 40 mg triamcinolone acetonide (Artropan), 132 2 mL 1% lidocaine and 1 ml saline. For the control 133 group, a 5 mL solution containing 3 mL 1% lidocaine 134 and 2 mL saline solution was applied. PRP was pre-135 pared using the literature-based double spin method. A 136 total of 100 mL of blood containing 15 mL of sodium 137 citrate for clotting inhibition was collected for PRP un-138 der aseptic conditions. 139

Two centrifugations were performed to obtain 10 mL 140 of PRP (first at 1500 rpm for 6 minutes and second at 141 3500 rpm for 12 minutes). The PRP unit was divided 142 into 2 sections, each 5 mL; the first part was sent to 143 the laboratory for platelet count and concentration, and 144 the second part was used for injection after 30 minutes. 145 Prior to injection, the PRP was activated by adding 146 1 mL 10% calcium chloride. The preparation method 147 used showed that the platelet count per mL increased 5-148 fold on average relative to baseline blood values [12]. 149 Patients were evaluated at baseline and then at 150 3 weeks, 12 weeks and 24 weeks after treatment. The 151 VAS, ASES and the WORC scores were used. The pa-152 tients scored their pain during abduction and adduc-153 tion movements on the VAS (0 = no pain; 10 = worst154 pain). The ASES, one of the most recent evaluations 155 for the shoulder, consists of two parts in which pain 156 (50 points) and function (50 points) are evaluated. For 157 pain, a 0–50 mm scale is used where 0 is unberrable 158 pain and 50 is pain. Function is evaluated as rohews: 159 0 unable; 1 with help; 2 with difficulty; 3 mild impact 160 and 4 normal. The WORC is an assessment scale de-161 veloped by the World Health Organization (WHO) that 162 includes 21 items representing 5 sub-cales (physical 163 symptoms, sporting activity, work, lifestyle and emo-164 tions) to measure the quality of life of patients with ro-165 tator cuff lesions. Each question is evaluated on a scale 166 of 0–100 mm and patients score between 0 and 2100. 167 In this study, volunteers were asked to evaluate each 168 question on a scale of 0-10 mm instead of 0-100 mm. 169

2.1. Statistics 170

The Number Cruncher Statistical System 2007 171 (NCSS; Kaysville, UT, USA) was used for statistical 172 analysis. Descriptive statistical methods (mean, stan-173 dard deviation, median, first quarter, third quarter, fre-174 quency, percentage, minimum and maximum) were 175 used to evaluate the study data. The normal distribution 176 of quantitative data was tested with the Shapiro-Wilk 177 test and graphical investigations. In the comparison 178 of more than 2 groups of quantitative variables show-179

Table 1			
Demographic characteristics and clinic	cal features		
Age (years)			
Min-max (median)	27-75 (54)		
Mean \pm SD	52.11 ± 10.78		
Sex			
Female	77 (64.2)		
Male	43 (35.8)		
Height (cm)			
Min-max (median)	145-190 (165)		
Mean \pm SD	166.77 ± 9.63		
Weight (kg)			
Min-max (median)	48-100 (79)		
Mean \pm SD	77.39 ± 10.64		
Dominant hand			
Right hand	114 (95.0)		
Left hand	6 (5.0)		
Affected hand			
Right hand	88 (73.3)		
Left hand	32 (26.7)		
Duration of complaints (n. on. h)			
Min-max (median)	3-10 (4)		
Mean SD	4.87 ± 1.76		
MRI findings			
Rotator cut, tendinosis	77 (64.2)		
Rot tor cu. ^{cr} endinosis + partial rupture	37 (30.8)		
Rota.or cuff tendinosis + bursitis	6 (5.0)		

irg normal distribution, one-way analysis of variance and the Bonferroni correction were used. For comparson of the Friedman test and the paired comparisons, the Bonferroni Corrected Wilcoxon signed-ranks test was used. The Pearson chi-squared test and Fisher-Freeman-Halton exact test were used to compare the qualitative data. Statistical significance was accepted as p < 0.05.

3. Results

Demographic and clinical features of the patients are shown in Table 1.

No statistically significant difference was found between the age, sex, height, weight and BMI distributions of the cases or affected hand distributions, duration of complaints and distribution of MRI findings (p > 0.05).

Evaluation of VAS scores according to injection groups are shown in Table 2 and distribution of VAS scores by injection types are shown in Fig. 3. The VAS 198 score at 3 weeks was significantly lower in the COR 199 group than the PRP, PRO and lidocaine group (p =200 0.001; p = 0.001; p = 0.001; p < 0.01).201

In the PRP group, the decrease in VAS scores at 12 202 and 24 weeks, according to baseline VAS scores, were 203 statistically significant (p = 0.001; p = 0.001; p < 0.001; p <204

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VAS		Inje	ction types		Test value
	PRP $(n = 30)$	$\frac{1}{1} \operatorname{PRO}\left(n = 30\right)$	$\frac{1}{\text{COR} (n = 30)}$	Lidocaine $(n = 30)$	- p
Baseline					
Min-max (median)	4-7 (6)	4-8 (6)	4-8 (6)	4-7 (5.5)	
Mean \pm SD	5.63 ± 1.00	5.9 ± 0.88	5.63 ± 0.93	5.47 ± 0.86	^d 0.386
3rd week					
Min-max (median)	2-6 (5)	1-6 (4.5)	0-6 (2.5)	0-6 (5)	
Mean \pm SD	4.83 ± 0.95	4.37 ± 1.16	2.43 ± 1.81	4.23 ± 1.48	^d 0.001**
12th week					
Min-max (median)	2-5 (4)	2-7 (4)	0-6 (4)	1-6(4)	
Mean \pm SD	3.9 ± 0.99	4.27 ± 1.36	3.53 ± 1.41	3.87 ± 0.97	^d 0.367
24th week					
Min-max (median)	0-5 (3)	0-6(3)	0-6 (4)	1-6(3)	
Mean \pm SD	2.57 ± 1.19	3.1 ± 1.52	3.77 ± 1.41	3.2 ± 1.19	^d 0.005**
p	0.001**	0.001**	0.001**	0.001**	
Baseline – 3rd week	_	0.001**	0.001**	0.002**	
Baseline - 12th week	0.001**	0.001**	0.001**	0.001**	
Baseline - 24th week	0.001**	0.001**	0.001**	0.001***	
3rd week - 12th week	_	-	-	-	
3rd week - 24th week	0.001**	0.014*	0.022*	-	
12th week - 24th week	0.004**	0.014*	-		
°		VAS Sco	ore		
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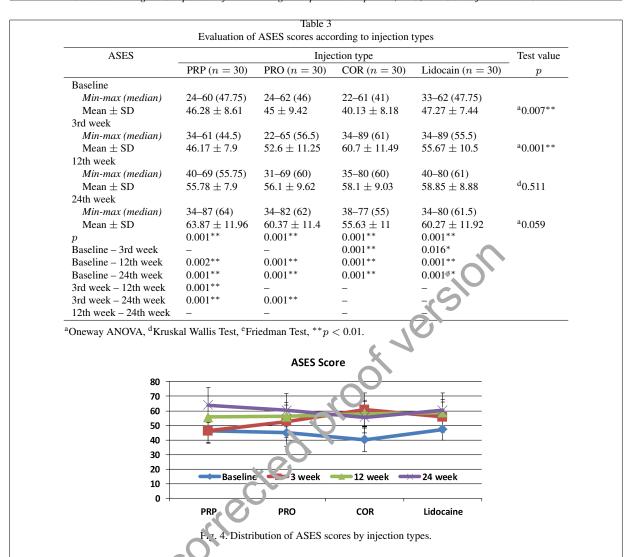
0.01). Similarly, decreases in VAS scores were found 205 to be statistically significeneat 12 and 24 weeks (p =206 0.001; p = 0.004; p < 0.01). In the PRO group, the 207 decrease in VAS scores at 3, 12 and 24 weeks were 208 statistically significant (p = 0.001; p = 0.001; p =209 0.001; p < 0.01). Similarly, decreases in VAS scores 210 at 24 weeks, compared to 3 and 12 weeks, were found 211 to be statistically significant (p = 0.014; p < 0.05). 212 In the COR group, the decrease in VAS scores at 3, 213 12 and 24 weeks were statistically significant accord-214 ing to baseline VAS scores (p = 0.001; p = 0.001; 215 p = 0.001; p < 0.01). In addition, the increase in VAS 216 scores at 24 weeks, compared to 3 weeks were found 217 to be statistically significant (p = 0.022; p < 0.05). In 218 the lidocaine group, the decrease in VAS scores at 3, 219 12 and 24 weeks were statistically significant accord-220

ing to the baseline VAS scores (p = 0.002; p = 0.001; p = 0.001; p < 0.01).

Evaluation of ASES scores according to injection groups are shown in Table 3 and distribution of ASES 224 scores by injection types are shown in Fig. 4. A statistically significant difference was found between the baseline ASES scores of the patients according to the injection type (p = 0.007; p < 0.01). According to Bonferroni test results, the baseline ASES score of the patients with a steroid injection type was significantly lower than the lidocaine group (p = 0.034; p = 0.008; p < 0.05). 232

The ASES score of COR group at 3 weeks was sig-233 nificantly higher than the PRP and PRO groups (p =234 0.001; p = 0.019; p < 0.05). The lidocaine group 235 ASES score at 3 weeks was significantly higher than 236 the PRP group (p = 0.003; p < 0.01). Additionally, the 237

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ASES scores of the COR group were not significant but were remarkably low ($_{F} = 9.059$; p > 0.05).

In the PRP group, the increase in ASES scores ac-240 cording to baseline was statistically significant at 12 241 and 24 weeks (p = 0.002; p = 0.001; p < 0.01). Simi-242 larly, the increase in ASES scores at 12 and 24 weeks, 243 according to ASES scores at 3 weeks, was statistically 244 significant (p = 0.001; p = 0.001; p < 0.01). In the 245 PRO group, the increase in ASES scores were found 246 to be statistically significant at 12 and 24 weeks, ac-247 cording to baseline (p = 0.001; p = 0.001; p < 0.01). 248 Similarly, the increase in ASES scores at 24 weeks, ac-249 cording to ASES scores at 3 weeks, were statistically 250 significant (p = 0.001; p < 0.01). In the COR group, 251 the increase in ASES scores at 3, 12 and 24 weeks, ac-252 cording to baseline ASES scores, were found to be sta-253 tistically significant (p = 0.001; p = 0.001; p = 0.001;254

p < 0.01). In the lidocaine group, the increase in ASES scores at 3, 12 and 24 weeks, according to baseline ASES scores, were found to be statistically significant (p = 0.016; p = 0.001; p = 0.001; p < 0.05).

Evaluation of WORC scores according to injection groups are shown in Table 4 and distribution of WORC scores by injection types are shown in Fig. 5. The WORC scores of the COR group at 3 weeks were significantly lower than the PRP, PRO and lidocaine groups (p = 0.011; p = 0.002; p = 0.002; p <0.05). The WORC scores at 24 weeks were significantly lower than the COR and lidocaine groups (p =0.047; p = 0.013; p < 0.05).

In the PRP group, the decrease in the WORC scores at 12 weeks and 24 weeks, according to the baseline WORC scores, were statistically significant (p = 0.001; p = 0.001; p < 0.01). Similarly, the decrease

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WORC	Injection type				
	PRP $(n = 30)$	PRO $(n = 30)$	COR (n = 30)	Lidocain $(n = 30)$	p
Baseline					
Min-max (median)	34.29-61.9 (51.9)	31.43-64.76 (55.24)	38.57-68.1 (52.86)	35.71-65.24 (53.33)	
Mean \pm SD 3rd week	50.79 ± 6.48	53.67 ± 8.43	51.4 ± 7.73	52.13 ± 7.92	^a 0.505
Min-max (median)	42.38-61.9 (50.95)	33.33-60.48 (54.52)	24.76-60.95 (41.19)	26.67-63.33 (55.95)	
Mean \pm SD 12th week	51.65 ± 5.79	52.03 ± 7.79	41.97 ± 11.05	51.71 ± 9.71	^d 0.001**
Min-max (median)	24.76-61.9 (44.29)	26.19-64.29 (47.86)	27.14-65.24 (47.86)	33.33-61.9 (48.57)	
Mean \pm SD 24th week	42.83 ± 9.63	46.38 ± 9.01	46.14 ± 9.64	48.27 ± 7.38	^a 0.131
Min-max (median)	34-130 (82)	42-130 (93)	60-126 (92)	60-132 (91)	
Mean \pm SD	79.46 ± 24.09	91.27 ± 21.79	93.90 ± 17.94	96.55 ± 20.43	^a 0.012*
p	0.001**	0.001**	0.001**	0.001**	
Baseline – 3rd week	-	_	0.001**	-	
Baseline - 12th week	0.001**	0.001**	**	-	
Baseline – 24th week	0.001**	0.001**	0.001**	• 0.01*	
3rd week – 12th week	0.001**	0.048*	-		
3rd week – 24th week	0.001**	0.001**	0.001**	0.001**	
12th week – 24th week	0.001**	0.001**	0.001**	0.001**	
	70 60 50 40	WORC Sco	re T		
	30		1	~	
	20 Base	eline 🗨 3 week 🗖	🛏 12 week 🛛 🗯 24 w	eek	
	0 PRP	PRO	COR Lido	caine	

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in the WORC scores at 12 and 24 weeks, compared to the scores at 3 weeks, were found to be statistically 272 273 significant (p = 0.001; p = 0.001; p < 0.01). The increase at 24 weeks from 12 weeks was statistically sig-274 275 nificant (p = 0.001; p < 0.01). In the PRO group, the 276 decrease in WORC scores at 12 weeks and the increase 277 in WORC scores at 24 weeks, according to baseline 278 scores, were statistically significant (p = 0.001; p =279 0.001; p < 0.01). Similarly, the increase in WORC 280 scores at 12 weeks and the decrease at 24 weeks com-281 pared to scores at 3 weeks, were statistically signifi-282 cant (p = 0.048; p = 0.001; p < 0.05). In the COR 283 group, the decrease in WORC scores at 3 weeks and 284 the increase in WORC scores at 24 weeks, according 285 to baseline scores, were statistically significant (p =286 (0.001; p = 0.001; p < 0.01). The increase in WORC 287 scores at 24 weeks, compared to WORC scores at base-288

line, 3 weeks and 12 weeks, were statistically significant (p = 0.001; p < 0.05). The increase at 24 weeks, from 12 weeks, was statistically significant (p = 0.001; p < 0.01). In the lidocaine group, the increase in WORC scores at 24 weeks, compared to WORC scores at baseline, 3 weeks and 12 weeks, were statistically significant (p = 0.001; p < 0.01).

4. Discussion

This study was the first to compare short-term and long-term effects of three different injection applications on patients with a rotator cuff lesion with a control group for more than 3 months. According to the results, in rotator cuff lesion cases, corticosteroid injection showed a more significant improvement com-

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pared to the other injections at 3 weeks, according to
the VAS, ASES and WORC scores. At 24 weeks, how ever, PRP application showed a more significant im provement. No differences were observed between the
results of the injection types used in patient evaluations
at 12 weeks.

Resting, NSAIDs, physical modalities (therapeutic 309 ultrasound, laser, tens, etc.) and training rotator cuff 310 muscles with force and stretching exercise programs 311 are recommended for patients complaining of shoulder 312 pain [13]. Despite the advances in conservative treat-313 ment, cases of use injuries and tendinosis are diffi-314 cult to treat successfully in the long term. Recently, 315 injection-based therapies have been applied for muscu-316 loskeletal problems and rotator cuff tendinopathies, in-317 cluding steroid injection, PRP injection, dry needling, 318 prolotherapy and sodium hyaluronate. All of these 319 injection methods are controversial, and a complete 320 agreement has not been reached by the various authors 321 studying these methods [14,15]. 322

Corticosteroid administration is applied in various 323 shoulder problems [16,17] and is known to provide effective pain control in the short term [18,19]. The use 325 of corticosteroids should be applied at the end of a 326 careful evaluation due to the potential risks of collagen 327 collapse, muscle weakness and tendon rupture [20]. 328 For these reason we excluded partial ruptures higher 329 than grade I and total RC ruptures. In this study, cor-330 ticosteroid treatment was observed to be superior to 331 other methods in the short term, but not for the long 332 term. 333

PRP has been a treatment method that has gained 334 popularity recently due to the role of growth factors re-335 leased from platelets in tissue healing. Additionally, se-336 rious side effects of this treatment method have not yet 337 been reported [21–23]. The study demonstrated that 338 the effectiveness of PRF administration was less effec-339 tive than the corticosteroid application at the early eval-340 uation stage at 3 weeks. In a placebo-controlled study 341 conducted in 22 cases with subacromial impingement 342 syndrome, PRP was evaluated to be effective on shoul-343 der range of motion (ROM) and VAS scores in the 344 same way as exercise [24]. According to the results 345 of 20 cases of chronic rotator cuff tendinopathy, the 346 VAS and WORC scores showed no superiority to a 347 placebo [25]. In another study of 17 cases compar-348 ing dry needling with 2-dose PRP at 4-week intervals, 349 the superiority of PRP in patient complaints and pain 350 scores compared to dry needling was demonstrated 351 in bursal and articular tendinopathies [26]. Since this 352 study was a randomized controlled blinded study, the optimal administration dose and duration of the PRP activity could not be evaluated as a single injection was performed. However, single-dose PRP application was shown to have a statistically significant contribution to pain scores at the 24 week evaluation.

Prolotherapy application has shown to be effective 359 for lateral epicondylitis, achilles tendinopathy, plan-360 tar fasciitis, hand osteoarthritis, hip adduction tendini-361 tis and rotator cuff problems [27-29]. This method 362 has advantages that include easy application, cheap-363 ness, success of treatment and shortening of the reha-364 bilitation process [30]. Although different agents like 365 sodium morrhuate and phenol glycerin are used, hy-366 perosmolar dextrose is the most common irritant solu-367 tion used [31]. First investigated by Lee, prolotherapy 368 application was used retrospectively for non-traumatic 369 rotator cuff patients with complaints lasting longer 370 than 3 months, and patients were evaluated between 3 371 and 8 sessions at intervals of 2-4 weeks [32]. In an-372 other study using prolotherapy in cases of rotator cuff 373 tendinc oathy, .mprovements in long-term pain and pa-374 tient satisfaction were made, but no significant advan-375 tage vas shown when comparing prolotherapy patients 376 with he control group [33]. 377

In this study, local anesthetic injection in the control group was beneficial in rotator cuff lesions, although not superior to other methods. There are similar studies in the literature, which may be due to the carryover effect of local anesthesia, the placebo effect shown in many treatments in medicine, and the distension effect of a subacromial 5 mL injection or the natural course of the disease [34]. In the review, steroids were found to be effective in the short term compared to local anesthetics; no significant difference was found between them in the long term. This confirmed that local anesthetics were effective as well [35].

The most important limitations of this study were 390 the small sample size, the use of prolotherapy and PRP 391 as a single injection and the relatively short duration of 392 follow-up. Therefore, studies with more than one in-393 jection of the same injection type with a longer follow-394 up period are needed. According to the results of the 395 ASES, WORC and VAS scores, steroid injection was 396 more effective for pain, function and quality of life in 397 patients with rotator cuff problems, whereas PRP in-398 jection was prominent in this study compared to other 399 injections for long-term well-being. Prolotherapy ap-400 plication at 3, 12 or 24 weeks compared to other meth-401 ods did not show significant superiority. In all types of 402 injections, improvement in pain, function and quality 403 of life were observed. 404

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5. Conclusion 405

No clear consensus can be found on the frequency 406 with which an injection is preferred. As reported by 407 some authors, the efficacy of multiple injections of the 408 same injection on rotator cuff pathologies may also be 409 a matter of future studies [36]. While the short-term re-410 sults of corticosteroid injection for the treatment of ro-411 tator cuff lesions did not respond to conservative treat-412 ment and were significantly superior to those of PRP, 413 this study concluded that the long-term success of PRP 414 injection was high, but all methods used, including li-415 docaine, could be beneficial for treatment. 416

Acknowledgments 417

The authors would like to thank everyone who par-418 ticipated in this study. 419

Conflict of interest 420

None to report. 421

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