MEDICAL SCIENCE MONITOR

CLINICAL RESEARCH

e-ISSN 1643-3750
© Med Sci Monit, 2020; 26: e919166
DOI: 10.12659/MSM.919166

Received: 2019.08.04
Accepted: 2019.11.18
Available online: 2020.01.21
Published: 2020.02.11

Treatment of Osteoarthritis Secondary to Developmental Dysplasia of the Hip with Prolotherapy Injection versus a Supervised Progressive Exercise Control

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

ABCD 1 Deniz Gül
ABEF 2 Aydan Orsçelik
ABCDEF 1 Serkan Akpancar

1 Department of Orthopedics Surgery, Tokat State Hospital, Tokat, Turkey
2 Department of Sports Medicine, Health Sciences University Gulhane Medical Faculty, Ankara, Turkey

Corresponding Author: Aydan Orsçelik, e-mail: aydan.orscelik@sbu.edu.tr
Source of support: Departmental sources

Background: Osteoarthritis secondary to developmental dysplasia of the hip (DDH) is one of the major causes of hip pain and disability. The aim of the study was to compare the effectiveness of prolotherapy (PrT) injections versus exercise protocol for the treatment of DDH.

Material/Methods: There were 46 hips of 41 patients who had osteoarthritis secondary to DDH included in this study. Patients were divided into 2 groups: treated with PrT (PrT group; n=20) and exercise (control group; n=21). Clinical outcomes were evaluated with visual analog scale for pain (VAS) and Harris hip score (HHS) at baseline, 3 weeks, 3 months, 6 months, and a minimum of 1-year follow-up. In PrT group clinical results were also compared in Crowe type I–IV hips.

Results: Between group analysis revealed no significant between group differences at baseline. Dextrose injection recipients out performed exercise controls for VAS pain change score at 6 months (–4.6±2.6 versus –2.8±2.5; *P*=0.016), and 12 months (–4.5±2.4 versus –2.9±2.5; *P*=0.017) and for HHS at 6 months (24.2±14.0 versus 14.8±12.4; *P*=0.007) and 12 months (24.3±13.4 versus 16.5±11.3; *P*=0.018).

Conclusions: To our best knowledge, this study is the first regarding the effects of an injection method in the treatment of osteoarthritis secondary to DDH. According to our study, PrT is superior to exercises. PrT could provide significant improvement for clinical outcomes in DDH and might delay surgery.

MeSH Keywords: Hip Dislocation, Congenital • Hip Joint • Injections • Osteoarthritis, Hip • Regenerative Medicine • Treatment Outcome

Full-text PDF: https://www.medscimonit.com/abstract/index/idArt/919166

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Background

Developmental dysplasia of the hip (DDH) is characterized by abnormal development of the hip joint, resulting in joint pain and destruction of articular cartilage along with loss of function and reduction in quality of life [1]. Various conservative and operative options are available for the treatment of DDH. Conservative modalities including weight loss, lifestyle modification, joint injections, and physical therapy in patients who have mild symptoms and mild destruction to relieve pain, preserve the hip, and delay the progression [2]. For advanced-stage painful hips, surgery seems to be the only method.

The muscles around the hip joint play an important role in providing load balance and keeping the femoral head in the acetabulum [3–5]. Many authors proposed that some muscle–tendon-related abnormalities accompany DDH. Iliopsoas, gluteus medius/minimus, and adductor tendons weaken by time. All these muscles have maximum stabilizing acts in the hip joint. Therefore, the result of an imbalance of these muscles may lead to overabundant stress on the labrum in the dysplastic hip joint, increase degenerative changes and result in worsening of the disease [6].

Various injection types and methods are available in the literature for different hip pathologies [7,8]. Prolotherapy (PrT) is an injection method successfully used in the degenerated and damaged joint structures including tendons, cartilage, and other connective tissues [9–15]. Previous studies have shown that dextrose has a neurogenic effect on pain at 5% concentrations [16,17], creates non-inflammatory ligament growth at 10% concentration [18] and, at more than 10% concentration, initiates a brief inflammatory cascade which promotes fibroblast growth and subsequent collagen production [19], and appears to be chondrogenic [20], thereby providing healing and tissue renewal.

Unlike other injection methods, PrT provides connective tissue healing around the joints. The efficiency of PrT in the management of DDH has not been evaluated so far. We hypothesized that PrT injections could provide healing and regeneration of the tissues around the hip joint, improve hip motions, correct the imbalance, and prevent degeneration.

The present study was carried out to evaluate the hypothesis that PrT injections are effective in reducing pain and improving function in the treatment of DDH. Therefore, we aimed to compare the efficacy of PrT and physiotherapy protocol in the management of DDH.

Material and Methods

Research design and patients

This is a study conducted to evaluate clinical results of PrT and exercise protocol for the treatment of osteoarthritis. In the study period beginning January 2016 thought October 2018, 46 hips of 41 patients with osteoarthritis secondary to DDH were divided into 2 groups using computer-derived random charts. All study protocols were approved by the Local Ethics Committee. Each patient included in the study signed an informed consent form. Patients whose ages varied between 18 years and 80 years, who had at least 6 months of symptomatic osteoarthritis secondary to DDH refractory to at least 3 months of standard care modalities (weight loss, temporary immobilization, use of analgesics and anti-inflammatory drugs, partial weight-bearing heel risers, orthotic provision, and physical therapy) and who had Crowe Type I–IV lesions in their standard anteroposterior hip radiographic and waiting list for total hip arthroplasty (THA) surgery at Tokat State Hospital were included in the study [21].

Patients with systemic or rheumatic diseases, active or chronic infection in the affected hip, hip problems accompanying DDH that may cause pain and loss of function in the hip and other chronic hip diseases, patients who had undergone surgery for joint preserving or arthroplasty of the hip, who had rheumatologic or neurological diseases that affect hip functions and pregnant patients were excluded from the study. The demographic and baseline characteristics of the patients are given in Table 1.

Intervention

In the PrT group, the injections were carried out under aseptic conditions using 23 G×3 ⅛ inch needles. Injections were made only in the problematic sites, and these sites were determined based on tenderness at physical examination. The depth and the location and of the injection points were monitored with ultrasound imaging; thus, a much smaller number of injections were performed. Injections were carried out in a supine and lateral decubitus positions.

Supine injection points

Injections were applied in supine position. A maximum of 8 mL dextrose solution (7.2 mL 15% dextrose and 0.8 mL lidocaine mixture) were injected into iliopsoas and adductor tendon insertions. In patients with type I and II DDH, a mixture containing 7.2 mL 25% dextrose and 0.8 mL lidocaine were applied to the hip joint with anterosuperior, parasagittal approach [22]. A proper needle position was confirmed by ultrasonographic visualization of the injected solution (Figure 1A).

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Table 1. Demographic features of the patients.

Variables	Group		*p*
	PrT	Control	
n	23 hips of 20 patients	23 hips of 21 patients	–
Gender (Male/Female)	8 male, 12 female	7 male, 14 female	0.185
Side (right/left/bilateral)	9/8/3	9/10/2	0.387
Age (years)	45.74±16.86	47.56±13.8	0.344
Duration of complaints (years)	9.57±3.09	9.34±2.67	0.399
Mean follow-up (months)	12.95±1.18	12.56±0.84	0.102
Mean injection sessions	5.26±0.92	–	
Crowe type	Type I (n=3); Type II (n=6); Type III (n=6); Type IV (n=8)	Type I (n=4); Type II (n=5); Type III (n=7); Type IV (n=7)	

Data are shown as mean±standard deviation or number; *p* – independent samples *t*-test or chi-square test were used.

Lateral injection points

The injections were applied in lateral decubitus position and the hip was in a neutral position. A maximum of 12 mL dextrose solution (10.8 mL 15% dextrose and 1.2 mL lidocaine mixture) were injected to gluteus medius, gluteus minimus insertions; then, the hip was given a flexion position for the piriformis insertion injection (Figure 1B).

In the post-injection period, the daily activities of the patients were not restricted, but patients were recommended to avoid intensive activity. Patients were instructed to take 500 mg of acetaminophen up to 4 times a day if necessary. The use of anti-inflammatory drugs was not allowed. Hot pack application to the injected areas was suggested 3 times a day during the first 3 days after the treatment. Injections were repeated with 21-day intervals. Injection sessions were terminated when the visual analog scale (VAS) scores decreased to 75% of pre-injection values. A maximum of 6 injection sessions was carried out unless the patient withdrew from the treatment. A home exercise program was given to patients according to the American College of Sports Medicine (ACSM) guidelines (3 times a day after 3 days of injections) [23].

Exercise protocol

In the control group, patients have received a rehabilitation protocol which was designed according to ACSM guidelines for progressive resistance training for healthy adults [23]. All patients received standard 12-week rehabilitation protocol and supervised progressive resistance training consisting of 30 training sessions (5 sessions per 2 weeks, an average of 45–60 minutes per season). All patients started with a warm-up on a stationary bicycle for 10 minutes. Then they performed leg press, hamstring curl and knee extension with double-legged, hip flexion with single-legged and lunges. Sets were performed 3 to 4 times with 8 repetitions. The intensity of all exercises increased progressively to a maximum of 12 repetitions. Eight repetitions of 3 sets were performed in the first 2 weeks and 4 sets in the last 2 weeks. If the sets were performed with 2 or more repetitions from the target of the maximum repetitions number, then the load was increased. All sessions were supervised by a physiotherapist or by a sports medicine physician to provide adequate loading and progression.

A home exercise plan with similar exercises 3 times a day was adopted to the patients for other days. Also, the home exercise plan was advised after the 12-week rehabilitation program.

Assessment and outcomes

A sports medicine (AO) performed follow-up evaluations of the patients at baseline, and 3 weeks, 3, 6, and 12 months after the first injection session. Pain intensity was scored using VAS, in which 0 meant no pain and 10 intolerable pain. Hip functions of patients were scored using Harris hip score (HHS), which measured a range of motion, deformity, and pain. HHS is one of the most commonly used tools for the evaluation of chronic hip pathologies [24]. Total scores range between 0 and 100 and higher scores indicate better functional results. As explained by Seven et al. the clinical outcomes were evaluated in 4 categories: excellent/good/fair/poor. Patients were assigned to appropriate categories based on pain intensity they experienced during daily activities, work or exercise.

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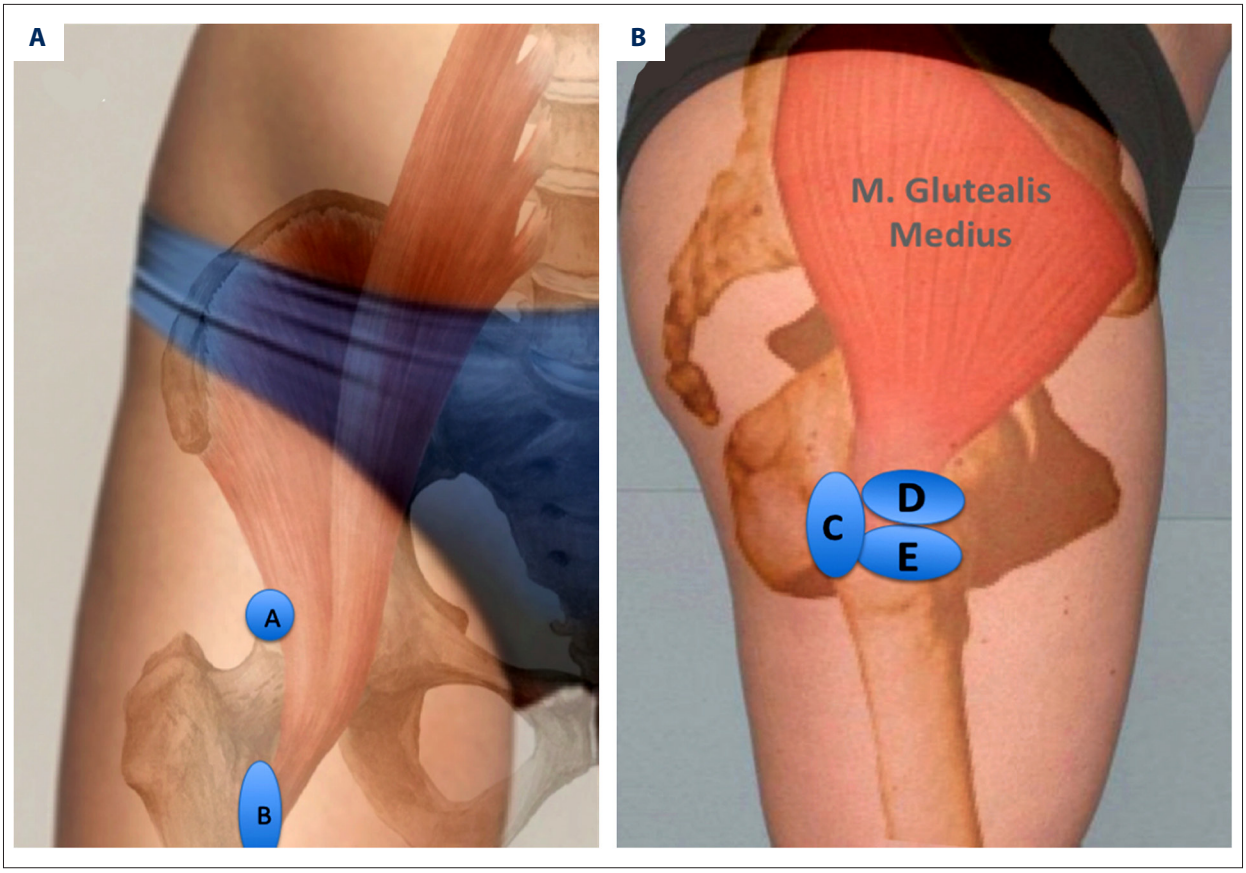

Figure 1. (**A, B**) Supine injection points; (A) intra-articular*, (B) iliopsoas and adductor tendon insertions. (C–E) Lateral injection points; (C) priformis insertion, (D) gluteus minimus insertion, (E) gluteus medius insertion.* Intra-articular injections were performed only to Type I and II hips.

"Excellent" meant no pain and a pain decrease of more than 50% compared to pre-treatment level was considered "good" while decreases between 25% and 50% were considered "fair" and decrease below 25% was "poor"[14].

Statistical analyses

Statistical analyses were actualized using IBM SPSS (version 25.0 for Windows). The data were presented as number, percent and mean±standard deviation (SD). According to Kolmogorov-Smirnov and Shapiro-Wilk normality analyzes, our values do not show normal distribution. Mann-Whitney U test, a non-parametric test for independent variables, was used for comparison of the groups. Wilcoxon test was used for within-group comparisons. $P<0.05$ was considered statistically significant.

Results

The present study included 46 hips of 41 patients. In both groups, pain reductions and functional improvement were statistically significant starting from day 21 through the end of the trial. VAS score decreased from 7.83±1.19 to 3.26±2.32 in PrT group, and from 7.43±1.12 to 4.52±2.35 in control group after 1 year of follow-up. HHS increased from 53.04±7.59 to 77.35±1 2.55 in PrT group, and from 51.91±5.71 to 68.8 3±11.21 in control group (Table 2). Based on between-group comparisons, pain reductions and functional improvement were statistically significant in the PrT group in comparison with the control group starting from day 21 through the end of the trial. The averages of the 2 groups were taken and are shown in Figure 2 according to the measurement periods. Especially the change in the first 21 days is noticeable. Changes in other periods show similar behavior.

The baseline and change scores for the VAS and HHS scores of the groups are shown in Table 3. Dextrose injection recipients outperformed exercise controls for VAS pain change score at 6 months (–4.6±2.6 versus –2.8±2.5; $P=0.016$), and 12 months (–4.5±2.4 versus –2.9±2.5; $P=0.017$) and for HHS at 6 months (24.2±14.0 versus 14.8±12.4; p=0.007) and 12 months (24.3±13.4 versus 16.5±11.3; $P=0.018$).

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Table 2. VAS and HHS scores of 2 study groups in different follow-up periods.

Measurements	PrT group	Control group	*p**
VAS_0	7.83±1.19[a]	7.43±1.12[a]	0.218
VAS_21 days	4.65±1.40[b]	5.52±1.08[b]	0.024
VAS_3 months	3.82±2.05[c]	4.82±1.64[c]	0.045
VAS_6 months	3.17±2.44[d]	4.56±2.33[c]	0.027
VAS_12 months	3.26±2.32[d]	4.52±2.35[c]	0.011
*p***	<0.001	<0.001	
HHS_0	53.04±7.59[a]	51.91±5.71[a]	0.683
HHS_21 days	69.91±7.94[b]	58.69±8.93[b]	<0.001
HHS_3 months	72.57±9.17[c]	64.17±10.51[c]	0.006
HHS_6 months	77.26±13.01[d]	66.74±13.10[c]	0.002
HHS_12 months	77.35±12.55[d]	68,47.83±11.21[c]	0.004
*p***	<0.001	<0.001	

* *p* – between-subject effect, ** *p* – within-subject effect. Means with the same symbol in columns are not significantly different. Between group comparison Mann Whitney-U; Within group comparison Wilcoxon. PrT – prolotherapy; VAS – visual analog scale; HHS – Harris hip score.

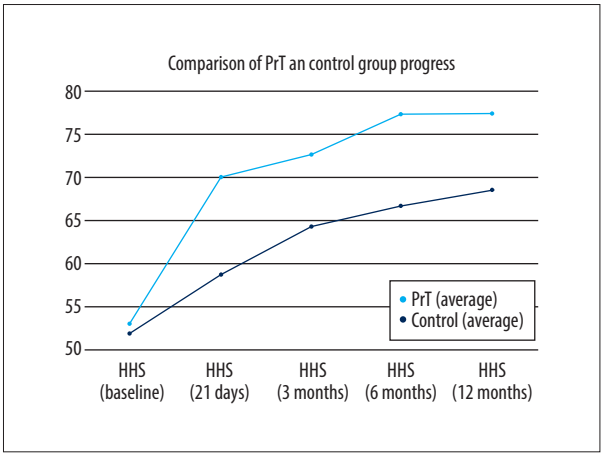

Figure 2. Comparison of prolotherapy (PrT) and control group progress

There was no significant difference between Type I, II, III, and IV hips in the VAS and HHS scores in the follow-up periods in the PrT group. In the PrT group excellent or good outcomes were achieved with 18 hips (78.3%) (excellent: n=7, good: n=12), while fair or poor outcomes were obtained with 5 hips (21.7%) (fair: n=2, poor: n=3) at the last follow-up. In control group excellent or good outcomes were achieved with 12 hips (52.1%) (excellent: n=1, good: n=11), while fair or poor outcomes were obtained with 11 hips (47.8%) (fair: n=4, poor: n=7) Serious complications such as cellulitis, septic joint arthritis, osteomyelitis or bleeding were not observed in any patient. Only 3 patients in the PrT group had severe pain in the injection sites and they took acetaminophen 4 times/day for 5–7 days after injections. The other patients did not describe pain or described mild pain and if they had pain, they took acetaminophen once a day for 3 days.

Discussion

DDH is an important hip problem, which considerably decreases the patient's satisfaction and comfort. There is limited evidence regarding the use of injection methods for DDH treatment in the literature. In the present study, the efficacy of the PrT was evaluated the first time in the literature. The results showed that PrT provides improved clinical outcomes and hip functions.

The muscles around the hip joint (musculus iliopsoas, gluteus medius, and minimus) are thought to be crucial in stabilizing the hip joint in patients with DDH due to shallow and steep acetabular roof [6]. Gluteus medius is the hip adductor group muscle that plays an essential role in balancing the abduction force around the hip joint like other abductor muscles of the hip (musculus piriformis, tensor fascia lata, gluteus maximus, and minimus) [25]. Failure of gluteus medius muscle results in losing pelvic control and the ability to walk (Trendelenburg sign). This is a condition known to surgeons and they are extremely careful to protect gluteus medius muscle during hip surgeries. Liu et al. [26] evaluated gluteus medius of 19 adults with unilateral DDH using computed tomography, and concluded that cross-sectional area, radiological density and the length of gluteus medius were significantly reduced. The activation angle of gluteus medius significantly increased and the

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Table 3. Baseline and change scores for pain and function.

Group	Baseline value (SD)	Change scores			
		21 days	3 months	6 months	12 months
Pain 0–100 VAS; mean (SD)					
PrT group n=23	7.8 (11.9)	−3.1 (1.2)	−4.0 (1.8)	−4.6 (2.6)	−4.5 (2.4)
Control group n=23	7.4 (11.2)	−1.9 (0.9)	−2.6 (1.9)	−2.8 (2.5)	−2.9 (2.5)
Function 0–100 HHS; mean					
PrT group n=23	53.0 (7.5)	+16.8 (7.3)	+19.5 (8.9)	+24.2 (14.0)	+24.3 (13.4)
Control group n=23	51.9 (5.7)	+6.7 (6.2)	+12.2 (8.6)	+14.8 (12.4)	+16.5 (11.3)

Dextrose injection significantly out-performed the control injection in pain improvement from 0–21 days (P=0.001), 0–3 months (P=0.008), 6 months (P=0.016) and 0–12 months (P=0.017), in dysfunction improvement from 0–21 days (P<0.001), 0–3 months (P=0.006), 6 months (P=0.007) and 0–12 months (P=0.018). PrT – prolotherapy; VAS – visual analog scale; HHS – Harris hip score; SD – standard deviation.

hip abductor moment arm decreased. The iliopsoas stabilizes the hip at anterior and conjoint with the hip capsule close to the capsule-labral complex [27,28]. Domb et al. reported that 18% of patients with symptomatic hip dysplasia had muscle–tendon-related abnormalities in the iliopsoas tendon determined in hip arthroscopy [29]. Jacobsen et al. [6] evaluated patients with unilateral and bilateral hip dysplasia with musculoskeletal ultrasonography and concluded that pain in these patients was concerned with both iliopsoas and the gluteus medius and minimus. In that study, tendon-related abnormalities were identified in iliopsoas tendon in 50%, in adductor longus tendon in 31% and gluteus medius/minimus tendons in 27% of the patients [6]. We thought that rehabilitation and regeneration of these tendons around the hip joint might improve the hip motions, correct the imbalance and prevent degeneration. Even after total hip arthroscopy, the most commonly used and effective scoring is HHS [30]. That's why we chose HHS in our study.

Unlike other proliferative injection methods, PrT can be performed intra-articular and/or peri-articular [8]. Thus, proliferation and healing can be achieved in intra- and peri-articular structures that will improve the stability of hip and its motility. Rehabilitation and home exercise programs have been found useful in the treatment of degenerative diseases in most studies [31,32]. In the present study, we used both intra- and peri-articular PrT injections and home exercise programs to achieve regeneration and strengthening of these muscles (iliopsoas, gluteus medius/minimus, and adductor tendons), and to improve hip functions and prevent degeneration. In parallel to our findings, a combination of PrT and home exercise programs was adopted for patients in most studies using PrT [12–14]. We concluded that the home exercise program made a considerable contribution to the success of the injections. Also, improvement in the control group revealed the benefit of exercise. However, the success of PrT and home exercise was superior to the control group in our study. Also, PrT and home exercise group showed a boast effect of pain and functional scores in the first 21 days of treatments and these high scores continuously increased till the end of the injections.

Various injection types and methods are available in the literature for different hip pathologies (hip osteoarthritis and femoroacetabular impingement); however, there is very limited evidence about the injection methods in the management of DDH [7,8,33]. In most of these studies, intra-articular injections were preferred, and platelet rich plasma, corticosteroids, hyaluronic acid were commonly used solutions. In the management of hip osteoarthritis, corticosteroids appear to be more effective than others due to meaningful pain relief for up to 12 weeks. However, it's believed to raise the risk of infection and chondrotoxicity. The use of corticosteroids tends to increase post-operative infection rates [34]. There is no consensus concerning intra-articular injections of hyaluronic acid and platelet rich plasma. In most studies, hyaluronic acid appears to be more efficient than platelet rich plasma, however, less efficacious than corticosteroids [33,35]. Similar to the aforementioned methods, intra-articularly applied PrT leads to regeneration in cartilage and intra-articular structures. Topol et al. [20] carried out arthroscopic biopsies in cases who underwent PrT. Biopsy analyses revealed activation in cartilage structures, cartilage regeneration along with variable cellular organization, fiber parallelism, and fibro- and hyaline-like cartilage typing patterns. In animal studies showed an increased inflammatory reaction and considerably enlarged ligament or cartilage structures at injection sites after PrT [36,37]. In our clinical experience, we generally use PrT as a proliferative injection method for similar indications. In the present study, 78.3% of the patients had excellent or good outcomes with PrT injections.

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Because of the false articulation of hip joint in Crowe Type III and IV hips, we used both intra- and extra-articular injections for only Crowe Type I and II hips and obtained similar clinical results. The use of similar methods and other injection types (hyaluronic acid, platelet rich plasma, stem cell therapy, etc.) in the treatment of DDH may increase the success rate. Therefore, future research efforts are needed to better evaluate the usefulness of the injection method in the management of DDH.

In the present study we used intra- and peri-articular PrT injections for the treatment of DDH as reported for the first time in the literature and our study obtained successful results. Fair or poor outcomes were obtained with only 4 hips (17.3%). We concluded that surgery was needed for these patients. We assume that rehabilitation of perifemoral muscles before the operation could make positive contributions to postoperative outcome in these patients. These results showed that proliferative injection methods could be useful for a high percentage of patients. However, only 12-month follow-ups in this study was not enough to understand the long-term effects of this treatment modality and to find out the percentage of patients for whom the treatment fails and who require surgery. The study patients were advised to continue their exercise program after the procedure and make yearly visits for follow-ups. In patients who subsequently experience pain and failure despite conservative treatments, additional injection protocols could be applied. Thus, protheses requirement might be delay for most of the patients.

Limitations of the study are its small sample size, relatively short follow-up period, and lack of a placebo control group.

Conclusions

This study is the first regarding the effects of an injection method in the treatment of osteoarthritis secondary to DDH. According to our study, PrT was superior to home exercises. PrT could provide significant improvement for clinical outcomes in DDH, and it might delay surgery. Therefore, more detailed studies with larger cohorts and longer follow-up periods could be useful.

Conflict of interests

None.

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