Gait Patterns after Intraarticular Treatment of Patients with Osteoarthritis of the Knee – Hyaluronan versus Triamcinolone: A Prospective, Randomized, Doubleblind, Monocentric Study

A. Skwara¹, R. Ponelis², C. O. Tibesku¹, D. Rosenbaum², S. Fuchs-Winkelmann¹

¹Department of Orthopaedics and Rheumatology, University Hospital Marburg, Marburg, Germany
²Department of Orthopaedics, Movement Analysis Lab, University Hospital Muenster, Germany
³Sportorthopaedicum Straubing, Straubing, Germany

Abstract

Objective: Evaluation of gait performance and muscle activity patterns as well as clinical efficacy and safety after single intraarticular injection with hyaluronan compared with triamcinolone in patients with knee osteoarthritis.

Materials and Methods: This trial evaluated the influence of a single injection of hyaluronan or triamcinolone on gait pattern and muscle activity. For clinical evaluation a visual analogue scale for pain, Lequesne index, and Knee Society Score were used. Quality of life was assessed with the SF-36.

Results: The complete analysis was performed in 50 of 60 patients. 26 patients were treated with triamcinolone and 24 with hyaluronan. Hyaluronan treatment led to significant improvement of range of motion at hip and knee. Significant improvement could be either demonstrated for the pain scale, Lequesne and Knee Society score in both groups. Quality of life showed greater improvement in the triamcinolone group. Quality of life showed improvement in the triamcinolone group.

Conclusion: Single application of high-viscosity hyaluronan shows superior range of motion and pain reduction as well as improvement in clinical results. Even if there was a lack of significant differences compared to triamcinolone, this therapy classified as safe and effective in the short follow up.

Key words: Osteoarthritis, Knee, Hyaluronan, Gait Analysis, Electromyography

Abbreviations: Osteoarthritis – OA, hyaluronan – HA, triamcinolone – TA, visual analogue scale – VAS, non-steroidal anti-inflammatory drugs – NSAID, non-animal stabilized hyaluronic acid – NASHA, standard deviation – SD, electromyography – EMG, Physical Functioning - PF, Role Physical - RP, Bodily Pain - BP, General Health Perceptions - GH, Vitality - VT, Social Functioning - SF, Role Emotional - RE, Mental Health - MH

Introduction

Osteoarthritis (OA) is the most common chronic joint disease of the aging patient [9]. The primarily affected joints are the knee and hip. The progress of the disease has an important influence on the patient’s life, including functional and social activities, body image and emotional well being [5]. Furthermore, socioeconomic aspects play an eminent role in the treatment of osteoarthritis in joints [28].

In non-operative treatment, pain reduction and improved function are the primary goals. It is important to distinguish between systemic and local therapeutic options. In the systemic treatment, palliation of pain can be achieved by simple analgetics, non-steroidal anti-inflammatory drugs and opioids. Local therapy can selectively treat the symptomatic joint. Intraarticular application of different drugs by injection can be performed. Glucocorticoids are the most commonly used intraarticular agents, which reduce pain and improve function and well being [23]. In recent years, the intraarticular use of different hyaluronan (HA) products became more widely accepted. Hyaluronan is a physiological component of the synovial fluid and cartilage matrix. It is responsible for the viscoelastic properties of the synovial fluid. In osteoarthritic joints, the molecular weight and the concentration of endogenous HA are decreased compared with healthy joints [6]. This implies a reduction of the viscoelasticity of the synovial fluid. In order to restore this viscoelasticity, augment the flow of the synovial fluid, normalise the synthesis and inhibit the degradation of endogenous hyaluronan, an application of exogenous HA can be performed [22]. The therapeutic effects and the safety of intraarticular application of HA in the treatment of OA in the knee have been demonstrated in several clinical trials [2, 8, 13, 21, 24, 25, 29]. Until now there are only three studies that objectively analysed few aspects of the functional outcome after treatment with HA.

The aim of this study was to analyse the difference of the functional and clinical outcome after intraarticular treatment of patients with osteoarthritis of the knee with a single injection of hyaluronan (HA) or Triamcinolone (TA) with respect to the quality of life during the study period. The main focus of our investigation was the functional assessment with clinical gait analysis and static and dynamic electromyography of knee joint stabilizing muscles in addition to safety issues and clinical results of the therapy.
MATERIAL AND METHODS

PATIENTS

Sixty patients with radiographically verified degenerative osteoarthritis of the knee were included. This investigation was approved by the local ethic committee (Arztekammer Westfalen Lippe: Reg.Nr. 311 Fuchs) and an informed consent was obtained from all participants.

The inclusion criteria were: men and women between 35 and 80 years of age, radiographically verified degenerative osteoarthritis of the knee (grade II or III according to the Kellgren and Lawrence classification) pain of at least 40 mm on a 100 mm visual analogue scale (VAS) at initial examination, persistent pain for at least 6 months, a Lequesne-Score of at least 10 points, good physical and mental status, good compliance and agreement to participate in this study [11, 15, 18].

Exclusion criteria were: patients with non-degeneratively induced osteoarthritis, rheumatoid arthritis, ligationous instability or complete resection of the meniscus, Sudeck’s disease, operations of the affected knee within the last three months, varus or valgus deformity of more than 15 degrees, patellofemoral arthritis, intraarticular therapy of the affected joint within the last 6 months with hyaluronan and three months with glucocorticoids, severe systemic diseases (tumor, exacerbated diabetes mellitus, hyperthyroidism), anti-thrombotic medication or regular medication with NSAID/psychiatric pharmaceuticals, infectious diseases, alcohol abuse, drugs, psychiatric diseases or suicidal tendencies, involvement in another study, non-compliance, acute haemorrhage or joint effusion, allergic predisposition, skin infections or skin diseases around the knee.

STUDY DESIGN

The study was a prospective, randomized, monocentric, patient- and observer-blinded clinical trial. With a computer-assisted randomisation, the patients were assigned to the respective therapy. Each therapy group consisted of 30 patients. The patients received one intraarticular injection of hyaluronan (HA) (3 ml, Durolane®, 20 mg/ml non-animal stabilized hyaluronic acid (NASHA) in buffered physiological sodium chloride solution pH 7 in one pre-filled glass syringe in sterile pack; Q-Med AB, Seminatievetan 21, SE-752 28 Upplandsviken, Sweden) or triamcinolone (TA) (1 ml, Volon A10®, 10mg triamcinolone acetonide, 10mg/ml; Bristol-Myers Squibb GmgH, 80632 München, Germany).

The mean study period was 104 (SD = 14.4) days for each patient. This period included the screening visit and the wash-out period of previous medication for two weeks if necessary, one injection of HA/TA and one follow up visit, 12 weeks after the injection.

WASHOUT AND ESCAPE MEDICATION

To evaluate the efficacy of pain reduction, anti-inflammatory and analgetic medication was terminated two weeks before the first injection of the test drugs. During the wash-out period, the patients were allowed to use paracetamol of up to 2 g/day. Further 100 mg/day acetylsalicylic acid were allowed for patients with cardiovascular diseases.

Use of the salvage medication was recorded in the patient’s diary. Patients with a higher usage of the allowed medication or medication with other analgetics were excluded of the study and were not substituted.

ASSESSMENTS

After checking the inclusion criteria and inclusion in the study, all study relevant data of the patients were recorded in the screening visit. The radiographic grade of osteoarthritis was classified according to Kellgren and Lawrence [15]. If the patients were using a medication that did not conform to the study design a wash-out period of two weeks was induced. After a wash out period as well as in the follow-up visit an instrumented gait analysis and electromyographic examination were performed.

For the instrumented gait analysis reflective markers were applied according to the Helen-Hayes marker set. The marker movement was recorded with a six camera system (Motion Analysis Corporation, Santa Rosa, USA). Ground reaction forces were recorded with two force platforms embedded in the walkway (Advanced Mechanical Technology, Inc., Watertown, MA, USA).

The electromyographic activity patterns during walking were recorded with bipolar surface electrodes from the following knee stabilizing thigh and shank muscles: rectus femoris, vastus medialis, vastus lateralis, semitendinosus, long head of the biceps femoris, tibialis anterior and medial gastrocnemius. Electrodes were positioned at defined anatomical landmarks according to the SENIAM recommendations [10] on the affected and contralateral extremity. The skin was cleaned and prepared (Nuprep Abrasive Skin Prepping Gel, Orlimed GmbH, 70780 Filderstadt) and self-adhesive, pre-gelled electrodes (Blue Sensor, Medicotest Oelstykke, Denmark) were attached to the marked locations on the skin. The EMG signals were amplified with a gain factor of 1000 and A/D converted and stored with 1000 Hz per channel and 12 bit resolution (MyoSystem 2000, Noraxon, Scottsdale, Arizona).

EMG activity patterns of at least 20 gait cycles were recorded and the initial contacts of the left and right foot were manually marked with two switches. These markers were used to subdivide the recordings into single gait cycles that were time normalized and averaged after root-mean-square rectification over 50 data points (MyoResearch, Noraxon, Scottsdale, Arizona, USA). Mean and maximum EMG amplitudes were determined from these averaged EMG signals.

Furthermore, the visual analogue scale for pain (VAS) [11], Knee Society Score (KSS) [12] and Lequesne Score [18] were used for clinical evaluation. Supplementary quality of life was quantified at each visit with the SF-36 health questionnaire [4].

STATISTICAL METHODS

The statistical analysis was performed for the two different treatment groups as well as for each treatment group themselves and intraindividual analysis of af-
fected and non affected extremity. For more than two dependent parameters the Friedman-test and for two dependent parameters the Wilcoxon test was used. For two independent parameters the Mann-Whitney U test was used. All tests were performed with commercial software (StatView 5.0; SAS Inc., Cary, NC, USA).

RESULTS
Complete follow up data were obtained from 50 of 60 patients (83.3%). Demographic and clinical data of these 50 patients, who were included in the final evaluation, are presented in Table 1. At first the results of each group will be presented separately and afterwards the two groups will be compared.

Table 1. Demographic data of the HA and TA group.

|       | HA     | SD | TA     | SD | Significance |
|-------|--------|----|--------|----|--------------|
| Age [yr] | 60.92  | 10.43 | 61.81  | 10.53 | 0.8082       |
| Height [cm] | 169.71 | 8.77 | 170.98 | 8.50 | 0.6551       |
| Weight [kg] | 81.73  | 14.87 | 83.44  | 16.58 | 0.9768       |
| BMI [kg/m²] | 28.24  | 3.92 | 28.52  | 5.10 | 0.7049       |
| Gender [m:f] | 12:12  | 15:11 |        |      |              |

HA GROUP
Twenty four patients of the HA group were included in the final analysis. Six patients were excluded because they canceled the participance in the study due to persistent knee pain without a benefit after the injection or a necessity of another therapy. In the 30 injections performed in this group we did not register any adverse reaction.

Instrumented gait analysis showed improvement of the mean values especially for stride length, walking speed and range of motion of the hip and knee. For the parameters maximum hip flexion (p = 0.0177), hip range of motion (p = 0.0043) and knee range of motion in stance (p = 0.0425) a significant improvement in the two visits was found (Table 2). The electromyographic examination of the lower extremity muscles did not reveal significant changes in the maximal voluntary contractions or in the muscle activity during gait. The only effect was seen in a significant decrease of the maximal EMG amplitude of the vastus lateralis muscle (p = 0.0163). Regarding the contralateral extremity not affected by gonarthrosis a similar muscle action was detected except for the gastrocnemius medialis muscle showing a significant increase of the maximal muscle activity (p = 0.0164) (Table 3 and 4). Differences between the affected and non-affected extremity could not be demonstrated either.

The clinical examination of the VAS for pain revealed a significant decrease in the HA group from 54.9 mm in the screening visit to 44.0 mm in the follow-up visit (p = 0.0416). The mean values of the Lequesne Score improved significantly in the HA group from 11.9 points in the screening visit to 10.1 in the follow-up visit (p<0.0001). The KSS showed in the subscales Knee-Score and Function-Score as well as in total KSS an improvement of the mean values from the screening to the follow-up visit. A significant improvement could be demonstrated for the subscale Knee-Score and the total KSS (Table 5).

The evaluation of the SF-36 health questionnaire in the HA group revealed an improvement of the mean values especially for the parameters physical role (RP) and emotional role (RE). Significant improvements were not found for any parameter (Fig. 1).

TA GROUP
In the TA group 26 of 30 patients were included in the statistical evaluation. Four patients were excluded. Two patients terminated the participation in this study because of persistent knee pain and the necessity of other therapy, one patient was excluded because of disc prolaps with the need of non-allowed medication and a need for a hospital treatment and the fourth patient was excluded because of persistent pain and knee joint effusion and the necessity of non-study-conforming therapy. An infection of the knee could be excluded by an aspiration. In the 30 injections performed in the TA group there were no complications or adverse reactions.

In the instrumented gait analysis of the TA group a significantly shorter stance phase (p = 0.0258) and longer swing phase (p = 0.0258) were evident (Table 2). Further noticeable differences of gait patterns
Table 2. Results of gait patterns of HA and TA group.

|                  | HA-Group |                | TA-Group |                | Significance |          |          |
|------------------|----------|----------------|----------|----------------|--------------|----------|----------|
|                  | Visit 1  | Visit 2        |          |                | Significance |          |          |
|                  | Mean     | SD             | Mean     | SD             | Mean         | SD       | Mean     | SD       | p-value   |
| Stride Length (cm) | 63.96   | 6.52           | 64.60    | 6.70           | 63.19        | 9.12     | 64.71    | 8.67     | 0.3606    |
| Walking Speed (m/s) | 116.85  | 16.96          | 119.31   | 17.71          | 115.03       | 20.44    | 113.96   | 18.15    | 0.3313    |
| Stance [% gait cycle] | 62.67   | 2.13           | 62.31    | 1.70           | 62.63        | 1.48     | 62.19    | 1.34     | 0.4405    |
| Swing [% gait cycle] | 37.33   | 2.13           | 37.69    | 1.70           | 37.37        | 1.48     | 37.81    | 1.34     | 0.4405    |
| Maximum Hip Flexion (°) | 38.74  | 7.91           | 42.48    | 6.19           | 36.16        | 6.78     | 38.33    | 8.87     | 0.0177    |
| Hip Range of Motion (°) | 45.66  | 3.37           | 47.49    | 4.38           | 45.03        | 4.80     | 46.17    | 4.30     | 0.0043    |
| Maximum Knee Flexion (°) | 59.65  | 5.12           | 59.67    | 3.28           | 58.20        | 5.69     | 58.15    | 6.20     | 0.9090    |
| Mid Stance Knee Flexion (°) | 16.82  | 6.80           | 18.20    | 5.74           | 18.80        | 5.19     | 19.24    | 5.71     | 0.1096    |
| Knee Range of Motion in Stance (°) | 12.53  | 4.40           | 14.10    | 5.56           | 13.81        | 5.62     | 14.15    | 5.09     | 0.0425    |
| Knee Range of Motion in Swing (°) | 55.36  | 6.70           | 55.56    | 5.70           | 53.0         | 7.78     | 53.06    | 7.03     | 0.0909    |
| Knee Abduction Moment Max 1 (Nm/kg BW) | 45.30  | 23.47          | 46.85    | 22.86          | 41.02        | 23.13    | 38.85    | 21.62    | 0.0627    |
| Knee Abduction Moment Max 2 (Nm/kg BW) | 35.42  | 23.56          | 37.76    | 23.38          | 28.98        | 17.10    | 31.10    | 17.58    | 0.2192    |
| Vertical Force Maximum 1 (% BW) | 105.55 | 8.67           | 106.08   | 10.23          | 107.03       | 10.47    | 107.83   | 8.77     | 0.4202    |
| Vertical Force Minimum (% BW) | 81.77  | 7.89           | 80.38    | 7.73           | 80.68        | 7.63     | 79.75    | 7.54     | 0.1572    |
| Vertical Force Maximum 2 (% BW) | 107.77 | 7.90           | 107.74   | 8.07           | 107.72       | 5.90     | 108.45   | 5.84     | 0.8415    |
Table 3. Results of electromyographic examination, maximal amplitude for the HA and TA group and the non-affected extremity.

| EMG Max [µV] | Affected Extremity | Non-affected Extremity |
|--------------|---------------------|------------------------|
|              | HA-Group | Significance | TA-Group | Significance | HA-Group | Significance | TA-Group | Significance |
|              | Mean | SD | Mean | SD | p-value | Mean | SD | Mean | SD | p-value |
| Visit 1      | 23.7 | 10.8 | 23.3 | 11.9 | 0.6476 | 26.3 | 18.3 | 25.3 | 18.9 | 0.7897 |
| Rectus femoris | 25.2 | 11.8 | 25.5 | 9.3 | 0.9772 | 27.2 | 21.3 | 24.4 | 14.9 | 0.5850 |
| Vastus medialis | 24.2 | 11.5 | 24.0 | 16.4 | 0.7533 | 28.5 | 19.4 | 28.0 | 21.1 | 0.5172 |
| Vastus laterals | 34.2 | 14.9 | 37.3 | 20.6 | 0.3758 | 43.0 | 26.1 | 42.1 | 23.1 | 0.6567 |
| Semitendinosus | 42.6 | 24.4 | 43.1 | 21.9 | 0.6892 | 41.8 | 19.2 | 43.8 | 25.7 | 0.8390 |
| Biceps femoris | 45.8 | 30.0 | 48.1 | 31.3 | 0.4929 | 42.4 | 26.1 | 40.9 | 23.5 | 0.7127 |
| Tibialis anterior | 98.3 | 51.9 | 87.6 | 39.5 | 0.2414 | 85.1 | 45.0 | 93.6 | 47.2 | 0.0962 |
| Gastrocnemius medialis | 31.6 | 15.5 | 35.4 | 27.5 | 0.9317 | 32.1 | 18.2 | 31.7 | 16.2 | 0.8192 |

Table 4. Results of electromyographic examination, maximal amplitude for the HA and TA group and the non affected extremity during gait.

| EMG Max [µV] | Affected Extremity | Non-affected Extremity |
|--------------|---------------------|------------------------|
|              | HA-Group | Significance | TA-Group | Significance | HA-Group | Significance | TA-Group | Significance |
|              | Mean | SD | Mean | SD | p-value | Mean | SD | Mean | SD | p-value |
| Visit 1      | 7.2 | 2.8 | 7.3 | 2.5 | 0.1888 | 6.6 | 2.3 | 6.8 | 2.2 | 0.3345 |
| Rectus femoris | 6.3 | 1.8 | 7.0 | 1.8 | 0.0503 | 6.0 | 1.4 | 6.3 | 1.8 | 0.5255 |
| Vastus medialis | 8.5 | 3.2 | 9.4 | 3.1 | 0.2087 | 9.0 | 3.7 | 9.5 | 3.5 | 0.3809 |
| Vastus laterals | 12.2 | 6.4 | 13.3 | 5.8 | 0.0503 | 12.4 | 5.7 | 13.7 | 5.9 | 0.0409 |
| Semitendinosus | 9.4 | 4.5 | 9.7 | 4.0 | 0.4073 | 10.5 | 4.5 | 12.9 | 7.1 | 0.0385 |
| Biceps femoris | 16.0 | 12.0 | 15.9 | 10.9 | 0.9658 | 12.7 | 6.8 | 12.7 | 5.5 | 0.7317 |
| Tibialis anterior | 41.6 | 9.8 | 47.4 | 13.0 | 0.0520 | 43.9 | 16.5 | 49.6 | 29.3 | 0.4237 |
| Gastrocnemius medialis | 16.9 | 8.0 | 18.0 | 7.3 | 0.2987 | 18.2 | 6.5 | 20.1 | 8.4 | 0.0536 |

| Easter 16, 2009 | 161 | 162 |
could not be evaluated, nor between the affected and non-affected extremity.

The electromyographic examination showed no changes of maximal EMG amplitudes neither for the affected nor for the non-affected extremity (Table 3).

The analysis of muscle activity during gait reveals in this group a significant improvement of the activity of the semitendinosus (p = 0.0385) and for the non affected extremity significant improvement for vastus lateralis (p = 0.0409) and medial gastrocnemius (p = 0.0032) (Table 4).

The results in the VAS for pain declined from 52.9 mm to 42.5 mm without a significance. In the Lequesne Score the TA group achieved a significant increase from 11.6 to 9.7 points (p<0.0001). Furthermore, the KSS showed a significant improvement in the knee subscale and for the total KSS score from 143.8 to 149.8 points (p = 0.0069) without a significance in the subscale function (Table 5).

The results of the SF-36 health questionnaire revealed an improvement especially for the parameters physical role (RP), bodily pain (BP), vitality (VT) and emotional role (RE). Impairment were revealed for the remaining parameters. The general health perception showed even a significant decrease from 62.3 to 56.5 points (p = 0.0065) (Fig. 1).

**Comparison of the HA and TA Group**

Comparison of the two groups revealed no significant differences for the gait analysis and electromyographic examination or for the clinical parameters and scores, even though significant improvements of several functional parameters and pain could be demonstrated in each group.

**Discussion**

In the present study the objective parameters of a computer-assisted gait analysis and electromyographic examination were evaluated in addition to clinical parameters and quality of life, after intraarticular treatment with hyaluronan and triamcinolone. A significant improvement of functional ability as determined by clinical gait analysis and electromyographic changes could only be demonstrated for a few parameters. However, further findings of this prospective, randomized, double-blind, monocentric study show a significant pain reduction, especially in the HA group, and significant improvement in the clinical scores in both study groups. Significant differences in functional and clinical efficacy between hyaluronan and triamcinolone could not be revealed.

The course of action of hyaluronan in the treatment of osteoarthritis is still unknown. In recent years, numerous studies evaluated the efficacy of hyaluronan. In spite of different study designs and application frequencies of hyaluronan with different molecular weights, several studies demonstrated that intraarticular viscosupplementation can sufficiently reduce pain, improve function and quality of life [1, 16, 20, 29]. However, there is no accurate consensus or recommendation for the mode of treatment with hyaluronan [3].

The main topic of this study was the examination of gait and muscle activity before and after treatment with single injection of high-viscosity hyaluronan. Three previous studies evaluated gait or muscle function after intraarticular treatment with hyaluronan. Miltner et al. reported about the influence of intraarticular treatment with hyaluronan on isokinetic muscle strength and total work measured with the Cybex 6000 [19]. They found a significant difference of peak torque and total work. As potential reasons for these changes the authors suggested pain reduction and better interaction of mechanoreceptors and nociceptors which improved joint mechanics and muscular function. Tang et al. performed two case-comparison trials and reported a significant increase of concentric and eccentric muscle strength and significantly improved gait patterns and improved ground reaction forces six weeks after HA treatment. Both measurements were performed one week after the last injection and the contralateral extremity was used as a control [26, 27]. Similarly, Yavuzer et al. reported a significant improvement of extensor and adductor moments, range of motion and GRF [30]. Noticeable and relevant gait pattern changes were seen in the improved hip and knee range of motion in the HA group. In all these studies hyaluronan was applied up to five times. In the present investigation with the single infiltration of hyaluronan, the electromyographic analysis did not reveal the expected changes of muscle function. The tendency of gait changes and EMG results is compa-
rable to the observations of Tang at al. [27]. In our investigation no significant improvement or a difference between the two experimental groups was seen. Both, the comparison with the contralateral extremity of the examined individual and the comparison with the control group could not demonstrate the differences for gait patterns and muscle activity.

The clinical results of our study revealed a significant and sufficient pain reduction in the VAS and an improvement in the Lequesne and KSS score, similar to other trials [13, 14, 17, 20, 25, 29]. An improvement of quality of life could also be demonstrated in both treatment groups for several parameters. At the follow-up visit, 12 weeks after intraarticular injection, hyaluronan showed a greater efficiency in pain reduction than triamcinolone. These results are in accordance with the results of other investigations that described a longer-lasting benefit of hyaluronan compared to triamcinolone and placebo treatment [8, 13, 14]. Therefore, the established loss of efficiency after a period of 5 to 13 weeks after application was the reason for the endpoint of this study with a 12 week follow-up after the last intraarticular injection [7, 8]. However, a major advantage of the hyaluronan drug used in this study is the frequency of application in comparison to other drugs since only a single application led to an improvement for 12 weeks. That implies an evidently lower risk of infection which can be caused by injecting the drug.

One of the eminent critical arguments in many trials is the high drop-out rate. This is one of the limitations of this study. The present drop-out rate in the HA group was due to persistent pain and led to reduction of the statistical power of this investigation. This problem, especially pointed out by Leopold et al. [17], plays an important role in study designs with a long follow-up and in comparison of efficiency.

In conclusion this study demonstrated that treatment with a single injection of high-viscosity hyaluronan can sufficiently reduce pain, improve knee function and enhance quality of life. Furthermore, this drug is safe and well tolerated. However, no significant improvement in gait and muscle activity patterns could be demonstrated in comparison with triamcinolone.

CONCLUSIONS

This investigation demonstrates the potency of hyaluronan in the treatment of osteoarthritis of the knee. Single application of high-viscosity hyaluronan shows only few significant improvements in the objective gait analysis for the intrapatient course. This is a disappointing result regarding to the conspicuous improvement of pain reduction as well as clinical results which were demonstrated once more. Even if there was a lack of significant differences compared to triamcinolone, the single injection of hyaluronan can be classified as safe and effective in the conservative treatment of osteoarthritis in the short follow-up, reducing the risk of infection due to the application frequency compared to other preparations. Further investigations are needed to verify the stadium related efficacy of hyaluronan to optimise this drug therapy.

REFERENCES

1. Altman RD, Akerman M, Beaulieu AD, Schnitzer TJ. Efficacy and safety of a single intra-articular injection of non-animal stabilized hyaluronic acid in patients with osteoarthritis of the knee. Osteoarthritis Cartilage. 2004 Aug;12(8):642-649.
2. Altman RD, Moskowitz R. Intraarticular sodium hyaluronate (Hyalgan) in the treatment of patients with osteoarthritis of the knee: a randomized clinical trial. Hyalgan Study Group. J Rheumatol. 1998 Nov;25(11):2203-2212.
3. Arrich J, Piribauer F, Mad P, Schmid D, Klaushofer K, Mullner M. Intra-articular hyaluronic acid for the treatment of osteoarthritis of the knee: systematic review and meta-analysis. CMAJ. 2005 Apr 12;172(7):1039-1043.
4. Bullinger M. German translation and psychometric testing of the SF-36 Health Survey: preliminary results from the IQOLA Project. International Quality of Life Assessment. Soc Sci Med. 1995 Nov;41(10):1359-1366.
5. Carr AJ. Beyond disability: measuring the social and personal consequences of osteoarthritis. Osteoarthritis Cartilage. 1999 Mar;7(2):230-238.
6. Dahl LB, Dahl IM, Engstrom-Laurent A, Granath K. Concentration and molecular weight of sodium hyaluronate in synovial fluid from patients with rheumatoid arthritis and other arthropathies. Ann Rheum Dis. 1985 Dec;44(12):817-822.
7. Dahlberg I, Lohmander LS, Ryd I. Intraarticular injections of hyaluronan in patients with cartilage abnormalities and knee pain. A one-year double-blind, placebo-controlled study. Arthritis Rheum. 1994 Apr;37(4):521-528.
8. Dougados M, Nguyen M, Liotrat V, Amor B. High molecular weight sodium hyaluronate (Hyalacort) in osteoarthritis of the knee: a 1 year placebo-controlled trial. Osteoarthritis Cartilage. 1993 Apr;1(2):97-103.
9. Felson DT, Zhang Y. An update on the epidemiology of knee and hip osteoarthritis with a view to prevention. Arthritis Rheum. 1998 Aug;41(8):1343-1355.
10. Hermens HJ, Bouter LM, Post A, van der Wouden JC, Bakker E, de Vet HC, Kester AD. In vitro comparison of two hyaluronan drugs and placebo in patients with knee osteoarthritis. A controlled, randomized, double-blind, parallel-design multicentre study. Rheumatology (Oxford). 2002 Nov;41(11):1240-1248.
11. Huskisson EC. Measurement of pain. Lancet. 1974 Nov 9;2(7889):1127-1131.
12. Insall JN, Dorr LD, Scott RD, Scott WN. Rationale of the Knee Society clinical rating system. Clinical Orthopaedics and Related Research. 1989 (248):13-14.
13. Jones AC, Patterson M, Doherty M. Intra-articular hyaluronic acid compared to intra-articular triamcinolone hexacetonide in inflammatory knee osteoarthritis. Osteoarthritis Cartilage. 1995 Dec;3(4):269-273.
14. Karlsson J, Stogren IS, Lohmander LS. Comparison of two hyaluronan drugs and placebo in patients with knee osteoarthritis. A controlled, randomized, double-blind, parallel-design multicentre study. Rheumatology (Oxford). 2002 Nov;41(11):1240-1248.
15. Kellgren JH, Lawrence JS. Radiological assessment of osteoarthritis. Ann Rheum Dis. 1957 Dec;16(4):494-502.
16. Kirchner M, Marshall DA. A double-blind randomized controlled trial comparing alternate forms of high molecular weight hyaluronan for the treatment of osteoarthritis of the knee. Osteoarthritis Cartilage. 2005 Oct;13(10):1335-1344.
17. Leopold SS, Redd BB, Warme WJ, Wehrle PA, Petris PD, Short S. Corticosteroid compared with hyaluronic acid injections for the treatment of osteoarthritis of the knee. A prospective, randomized trial. J Bone Joint Surg Am. 2003 Jul;85-A(7):1197-1203.
18. Lequesne MG, Mery C, Samson M, Gerard P Indexes of severity for osteoarthritis of the hip and knee. Validation-value in comparison with other assessment tests. Scand J Rheumatol Suppl. 1987 65:85-89.

19. Miltner O, Schneider U, Siebert CH, Niedhart C, Niethard FU Efficacy of intraarticular hyaluronic acid in patients with osteoarthritis—a prospective clinical trial. Osteoarthritis Cartilage. 2002 Sep; 10(9):680-686.

20. Petrella RJ Hyaluronic acid for the treatment of knee osteoarthritis: long-term outcomes from a naturalistic primary care experience. Am J Phys Med Rehabil. 2005 Apr; 84(4):278-283; quiz 284, 293.

21. Petrella RJ, Petrella MA A prospective, randomized, double-blind, placebo controlled study to evaluate the efficacy of intraarticular hyaluronic acid for osteoarthritis of the knee. J Rheumatol. 2006 May; 33(5):951-956.

22. Peyron JG A new approach to the treatment of osteoarthritis: viscosupplementation. Osteoarthritis Cartilage. 1993 Apr; 1(2):85-87.

23. Raynauld JP, Buckland-Wright C, Ward R, Choquette D, Haraux B, Martel-Pelletier J, Urhman I, Khy V, Tremblay JL, Bertrand C, Pelletier JP Safety and efficacy of long-term intraarticular steroid injections in osteoarthritis of the knee: a randomized, double-blind, placebo-controlled trial. Arthritis Rheum. 2003 Feb; 48(2):370-377.

24. Raynauld JP, Torrance GW, Band PA, Goldsmith CH, Tugwell P, Walker V, Schultz M, Bellamy N A prospective, randomized, pragmatic, health outcomes trial evaluating the incorporation of hylan G-F 20 into the treatment paradigm for patients with knee osteoarthritis (Part 2 of 2): clinical results. Osteoarthritis Cartilage. 2002 Jul; 10(7):518-527.

25. Tamir E, Robinson D, Koren R, Agar G, Halperin N Intra-articular hylanuron injections for the treatment of osteoarthritis of the knee: a randomized, double blind, placebo controlled study. Clin Exp Rheumatol. 2001 May-Jun; 19(3):265-270.

26. Tang SF, Chen CP, Chen MJ, Hong WH, Yu TY, Tsai WC. Improvement of muscle strength in osteoarthritic knee patients after intraarticular knee injection of hyaluronan. Am J Phys Med Rehabil. 2005 Apr; 84(4):274-277.

27. Tang SF, Chen CP, Chen MJ, Pei YC, Lau YC, Leong CP Changes in sagittal ground reaction forces after intra-articular hyaluronate injections for knee osteoarthritis. Arch Phys Med Rehabil. 2004 Jun; 85(6):951-955.

28. Torrance GW, Raynauld JP, Walker V, Goldsmith CH, Bellamy N, Band PA, Schultz M, Tugwell P A prospective, randomized, pragmatic, health outcomes trial evaluating the incorporation of hylan G-F 20 into the treatment paradigm for patients with knee osteoarthritis (Part 2 of 2): economic results. Osteoarthritis Cartilage. 2002 Jul; 10(7):518-527.

29. Waddell DD, Bricker DC Clinical experience with the effectiveness and tolerability of hylan G-F 20 in 1047 patients with osteoarthritis of the knee. J Knee Surg. 2006 Jan; 19(1):19-27.

30. Yavuzer G, Sonel B, Suldur N, Ergin S Effects of intraarticular hylan G-F 20 injections on clinical and biomechanical characteristics of the knee in osteoarthritis. Int J Rehabil Res. 2005 Dec; 28(4):371-374.

Received: February 22, 2009 / Accepted: March 12, 2009

Address for correspondence: Adrian, Skwara, MD Department of Orthopaedics and Rheumatology University Hospital Marburg Baldingerstrasse 35043 Marburg Germany Tel.: +49 6421 5863789 Fax: +49 6421 5867007 E-mail: skwara@med.uni-marburg.de