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RESEARCH ARTICLE

OBSERVATIONAL CLINICAL PRACTICE STUDY OF A SINGLE ADANT INJECTION IN RHIZARTHROSIS

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Abstract

Background: Rhizarthrosis, or osteoarthritis (OA) of the first carpometacarpal joint, is currently considered a common pathology, associated with aging,affecting approximately 7% of men and 15% of women over the age of 50.Despite its high prevalence, only a small number of patients seek medical attention.Adequate conservative treatment can alleviate symptoms and even reduce the need for surgery in up to 70% of cases. The possibilities of conservative treatment include intra-articular (IA) injection of corticosteroids and hyaluronic acid (HA). The efficacy of IA HA has been proven especially in knee but the data in rhizarthrosis are scarce.Most HAs had been registered as medical devices worldwide and the EU Medical Devices Regulation (MDR 745/2017) requires a continuous post-market follow-up to ensure the safety and performance of these products. In compliance with the MDR, this work aimed to evaluate the efficacy and the impact on quality of life, of a marketed HA, in a cohort of patients with rhizarthrosis under real conditions in clinical practice.

Methods: Observational, post-marketing, retrospective, follow-up study. Between January 2020/June 2022, patients were treated in the Rheumatology Dpt. of Hospital General Universitario de Elche, Spain,with a single injection of HA (Adant®, Meiji Pharma Spain) and followed for 6 months. Pre/post Visual Analogue Scale (VAS) for pain, and functional questions (key, grip and button) were used for efficacy assessment. Patients' data were pseudonymized and included in a database for further analysis. The chi^2 test was used, for qualitative variables, and the T or Mann Whitney tests for quantitative ones. The pre/post comparison of the VAS was made with the t test for paired samples. The study was approved by the Ethics Committee of the hospital.

Results: Twenty patients with a mean age of 61 years, 80% women, were studied. An 80% had bilateral rhizarthrosis, 70% had Kellgren-Lawrence gradeIII-IV (moderate-severe) and 65% had other chronic medical condition (e.g., hand OA, osteoporosis, diabetes, etc.).The 80% of the patients had received 2 previous treatments with HA injections. The volume administered varied from 1 to 2 ml (55%-45%). The mean absolute change from baseline in VAS pain score over 6 months was -5.95, a reduction of 77% ($p<0.001$). A 35% of the patients had an

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improvement≥80% and the others between 70 and 79%. Regarding functional capacities, the 80% of the patientsachieved complete recovery.No significant statistical correlations were observed between baseline characteristics, the number of prior injections, or the volume administered, and the degree of improvement in pain or functional outcomes.All patients were satisfied with the treatment. There were no adverse events recorded.

Conclusion: This study suggests that viscosupplementation using Adant is an effective and well tolerated therapeutic option in managing pain and improving function of rhizarthrosis with an excellent safety profile.

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Introduction:

Rhizarthrosis, or OA of the first carpometacarpal joint, is currently considered a common condition associated with aging, affecting approximately 7% of men and 15% of women over the age of 50.(1) Despite its high prevalence, only a small number of patients seek medical attention.(2)

Patients typically present with severe pain and functional impairment, and it has been shown that appropriate conservative treatment can alleviate symptoms and even reduce the need for surgery by up to 70% in some cases.(3)HA injections are included among the conservative treatment options.(4)

Viscosupplementation with IA HA injections for OA began in the late 20th century, aiming to restore altered synovial fluid.(5) Several studies have confirmed that HA interacts with inflammation mediators, reduces apoptosis in cartilage, stimulates chondrocyte growth, and enhances extracellular matrix protein synthesis.(5)Currently, it is a well-known and widely used treatment, particularly in knee OA, and is recognized by most scientific societies.(6–10)

In the case of rizartrosis, studies have shown functional improvements in patients with moderate to severe stages of the disease, with 3 HA injections spaced 7 days apart.(11) When comparing HA use with corticosteroids, although both treatments show symptom reduction in the early weeks, after six months, results are better with HA(12), also leading to a reduction in the use of Non-Steroidal Anti-Inflammatory Drugs (NSAIDs).(13)

Adant® is a biotechnological HA product manufactured by Meiji Pharma Spain (MPS), authorized in Europe in 1996 as a medical device for treating OA in various synovial joints.(14) Typically, it is administered intraarticularly once a week for 3-5 consecutive weeks.(15) In patients with knee OA, repeated administration of Adant® has been shown to have a cumulative "carry over" effect, extending symptom improvement for up to one year after the last injection.(16)

Available experience with Adant® demonstrates its efficacy in reducing symptoms and improving the quality of life in patients with rhizartrosis.(17,18) These results, along with an excellent safety profile, make the risk/benefit ratio highly favorable.(14)

Objective:

The objective is to follow a cohort of patients treated with Adant® for rhizarthrosis under real-world conditions. This study is part of the post-marketing surveillance of Adant®, in accordance with the EU MDR 745/2017.(19) This new regulation, which came into force in 2023, highlights the need to follow-up medical devices throughout their lifecycle to monitor their safety and efficacy.

Material and Methods:

Ethics

The study was authorized by the research ethics committee of the Hospital General Universitario de Elche and the waiver of informed consent was approved (approval code PI 79/2022). The study adhered to the Declaration of Helsinki. To ensure patient’s privacy, data were pseudonymized.

Study design
An observational, post-marketing, cross-sectional, and retrospective study in a cohort of patients with rhizarthrosis treated with Adant®.

Inclusion criteria consisted of adult patients with rhizarthrosis, confirmed radiologically, at least grade II according to the Kellgren-Lawrence classification, treated with Adant® at the Hospital General Universitario de Elche between January 1st, 2020, and June 30th, 2022, with a minimum follow-up period of 6 months under routine clinical practice. Additionally, patients were required to have a VAS pain score ≥4, before the treatment.The following information were obtained from patient's medical history: age, sex, severity of the infiltrated joint assessed by radiography (X-ray)according to the Kellgren-Lawrence classification,VAS pain score (baseline and after 6 months), chronic medical conditions, concomitant medicationfor rhizarthrosis, pathologies detected after HA injection(accidents, falls, or surgeries), infiltrated joint (left/right), administered volume (ml), previous HA injections and quality of life and satisfaction assessment questionnaire at 6 months after treatment (annex I).Patients for whom insufficient information was available were excluded from the analysis.

The above information was included in a database for subsequent statistical analysis. The data werepseudonymized and identified by a code, ensuring that no information could identify the patients. Once the data has been analyzed, a statistical report was prepared, whichserved as the basis for the subsequent publication of the results.

Outcomes measures
The VAS was used to measure pain. Pain measured by VAS consisted of a discrete scale from 0 (no pain) to 10 (maximum pain).

The quality of life and satisfaction assessment questionnaire was conducted as part of routine clinical practice during the patient's visit to the specialist to assess hand functionality and treatment satisfaction in patients with rhizarthrosis after six months of follow-up. The questions were completed by the physician during the interview to evaluate functional recovery in daily activities and the patient's subjective perception of treatment outcomes. While not part of a standardized tool, it included elements inspired by validated instruments such as Functional Index for Hand Osteoarthritis (FIHOA) and Michigan Hand Outcomes Questionnaire (MHQ).

Statistics
Descriptive Statistics
Qualitative variables were described using absolute frequencies and percentages. Quantitative variables that follow a normal distribution was described using mean, standard deviation (SD), minimum (Min), and maximum (Max); while those that do not follow a normal distribution was described using median, interquartile range (first quartile (Q1) – third quartile (Q3)), Min, and Max.

Analytical Statistics
Univariate comparisons between categorical variables were performed using the chi-square test and/or Fisher's exact test. For continuous variables, the shape of the distributions was analyzed using the Kolmogorov-Smirnov and Shapiro-Wilk tests. Comparisons between two unrelated means were made using the Student's t-test or the Mann-Whitney U test. In the case of analyzing more than two groups, comparisons were made using ANOVA or the Kruskal-Wallis test.

Results:

Study population: sociodemographic and clinical characteristics
The study included a cohort of 20 patients with a mean age of 63.1 years (SD = 7.76). The 80% of the patients (16) were women. The severity of rhizarthrosis was classified using Kellgren-Lawrence system, with the 55% of patients being grade III. All sociodemographic and clinical features were detailed in table 1.

Chronic medical condition
The chronic medical conditionpresented in the patients at the beginning of the treatment under study were registered, 13 patients (65%) had at least one comorbidity. Nine patients (45%) presented some osteoarticular pathology. Seven patients (35%) had no chronic medical condition. The main ones included hand OA and osteoporosis. (Table 2).

Previous treatment with hyaluronic acid
Regarding previous HA injections received by the patients for rhizarthrosis, 80% (16) of them had previously received a median of 2 injections. The 10% of the patients (2) received 3 injections, one patient received 4 injections, and another patient received 8 previous injections.

Treatment with hyaluronic acid in study
During the study, the patients received a HA injection for the treatment of rhizarthrosis as part of routine clinical practice. The 40% of the patients(8) received the treatment in both first carpometacarpal joints. The median injected HA volume was 1 ml. The 55% of the patients (11) received 1 ml, and the 45% (9) were injected with a volume of 2 ml.

Concomitant medication
All patients were undergoing additional treatments concomitantly with the administration of the HA injection as part of their overall therapeutic approach.Twelve patients (60%) were treated with NSAIDs, specifically etoricoxib. The concomitant medication during the study were summarized in the table 3.

Efficacy assessment
The mean baseline VAS score was 7.70 (SD = 1.17), and the mean final VAS score at 6 months was 1.75 (SD = 1.07) ($p < 0.001$), (figure 1).

All patients showed improvements in the VAS, with the smallest reduction being 28.6%. Reductions of at least 30% were considered clinically relevant. Only one patient did not achieve this improvement. This patient was a 62-year-old woman with rhizarthrosisKellgren-Lawrence grade II, who had received two prior treatment with HA. She presented with a baseline VAS score of 7, and from a functional perspective, she did not have problems with key handling, buttoning, or grip closure.

A reduction ≥80% in the VAS wasconsidered a highimprovement. This level of improvement was achieved by 35% of the patients (7) in the study. Thirteen patients showed an improvement in the VAS between 70% and 79%. The mean pain reduction was 77% in the study population ($p < 0.001$).

Regarding the recovery of joint functionality at 6 months, three questions were assessed (key handling, grip the fist, and buttoning), and it was recorded whether the patient was able to perform each activities or not. Sixteen patients (80%) demonstrated adequate functionality in all three activities at the 6-month follow-up, while 20% (4) showed partial improvement in joint functionality, achieving improvement in at least one of the three activities(table 4).

All the patients were satisfied with the HA treatment.

No predictive factors of response were identified among the variables measured in the study (basal characteristics, number of previous injections and volume administered) and the pain or function improvements of rhizarthrosis.

Safety
During the study, no adverse events were recorded. No patient developed any other significant health issues after receiving the HA injection, including accidents, falls, or surgeries.

Discussion:

The results of this study provide data on the management of rhizarthrosis with a single HA injection in real-world clinical practice.Currently, there is limited evidence compared to its use in knee OA.(6–10) Our findings suggest that HA injection into the first carpometacarpal joint could represent an effective treatment for improving pain and functionality in patients with rhizarthrosis, offering a less invasive option before considering surgical treatments.

Many studies have demonstrated the beneficial effects of HA in knee OA, with improvements in pain and joint function. However, extrapolating these results to rhizarthrosis is not straightforward due to biomechanical differences and variations in joint load.

Fuchs et al., conducted aprospective, controlled, randomized study assessed the efficacy and tolerability of IA HA and triamcinolone acetonide in 56 patients with OA of the carpometacarpal joint of the thumb over 26 weeks.

Patients received three injections. Results showed that triamcinolone acetonideprovided quicker pain relief at 2-3 weeks, while HA showed a slight superiority at week 26 and had significantly better lateral pinch power.(12) Heyworth et al. in a double-blind controlled trial, included 60 patients with basal jointOA. Patients were randomized to receive two injections of HA, one saline injection followed by a corticosteroid injection, or two saline injections. No statistically significant between-group differences in pain were observed, but significant improvements in pain compared to baseline at weeks 12 and 26 were seen in the HA group.(20)In the study of Figen et al., 33 women with bilateral thumb base OA were included and received single injection of HA in one hand, and saline in the other hand.Statistically significant improvements were detected in function ($p = 0.001$), VAS pain ($p = 0.002$), and pinch strength ($p = 0.004$) at the 24th week in the HA group. However, only VAS pain scores decreased temporarily in control hands at the 6th week ($p = 0.02$).(21)Bahadir et al conducted a randomized, open-label, evaluator-blinded clinical study including 40 women with stage II or III trapeziometacarpal joint OA. The steroid group ($n = 20$) received one injection of 20 mg triamcinolone acetonide once and the HA group ($n = 20$) received three injections of 5 mg HA at 1-week intervals. Pain level decreased significantly over 12 months for the steroid group and over 6 months for the HA group. Hand function improved in both groups but it was only significant in the steroid group. (22)Velasco et al. in a prospective, single-arm, multicenter, open-label study with a 6-month follow-up period included 35 patients with rhizarthrosis treated with a single HA injection. The least-squares mean change from baseline in VAS pain score over 6 months was –2.00, a reduction of 27.8% ($p<0.001$).(23)

These studies present promising results, though with limitations, including small sample sizes and methodological heterogeneity. Our findings align with the results of these studies, further supporting the potential efficacy of HA injections in the management of rhizarthrosis. Additionally, our data provide valuable insights into the real-world, contributing to the evidence and complementing existing knowledge.

The patients included in this study reported a high level of satisfaction with HA injection, highlighting significant improvements in pain and quality of life. Furthermore, no adverse events were recorded, suggesting an excellent safety profile for this treatment.This aspect is particularly important in long-term treatments for chronic conditions such as OA.Moreover, a favorable safety profile enhances both healthcare professionals' and patients' confidence in the treatment, contributing to better adherence and satisfaction.

Comparisons with clinical trials should be made with caution, as both the design and methodology of observational real-world studies differ substantially from those of randomized clinical trials. In this context, clinical trials typically limit or prohibit the use of prior HA injections, which may not reflect the real-world clinical practice. In our study, the majority of the patients included had previously received IA HA treatments.

On the other hand, our study has some limitations inherent to its retrospective nature and clinical practice design. Patients were managed at the discretion of the physician based on clinical practice, rather than according to a pre-established protocol. Additionally, the data were retrospectively collected from the available medical records, following the routine practice at the participating site. Knowledge of clinical practice is crucial for understanding how treatments are applied in real-world and how healthcare professionals make decisions based on experiences and outcomes. In the context of HA injections, this knowledge enables physicians to identify which patients may benefit the most, treatments to their specific needs, and improve health outcomes while ensuring adherence to best clinical practices based on scientific evidence.

Conclusion:

Six months after a single HA injection, all patients had benefited from treatment, either due to decreased pain, improved functional abilities, or both.

No predictive factors of response were identified among the variables measured in the study and the pain or function improvements of HA injection.

The safety profileof HA injections in clinicalpracticewas favorable and similar tothatpreviouslydescribed.

In conclusion, our findings suggest that HA injection could be an useful treatment in the management of rhizarthrosis, helping to improve pain and functionality with an excellent safety profile. However, further research is required to establish its long-term impact and its positioning within clinical guidelines.

Declarations

Ethics approval and consent to participate

The study was authorized by the research ethics committee of the Hospital General Universitario de Elche and the waiver of informed consent was approved (approval code PI 79/2022).

Consent for publication

Not applicable.

Availability of data and materials

The datasets used and analyzed during the current study are available from the authors on reasonable request.

Competing interests

MP. Coronel Granado and D. Acosta-Rubio are employees of Meiji Pharma Spain. Other authors do not have COI.

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Authors' contribution

Concept and design of the study: CGMP, NBF, NPJR
Collection of data: NBF, NPJR
Interpretation of the data: NBF, NPJR, ARD, CGMP
Drafting of the manuscript:ARD, CGMP
Critical revision and final approval: NBF, NPJR

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The statistical analysis and report were conducted by D. J.J. Granizo Martínez (Granadatos SL).

List of abbreviations

HA - hyaluronic acid
IA - intra-articular
IQR- Interquartile Range
Max - maximum
MDR - medical devices regulation
Min - minimum
MPS – Meiji Pharma Spain
NSAIDs - Non-steroidal anti-inflammatory drugs
OA – osteoarthrosis
Q1 – firstquartile
Q3 – thirdquartile
SD - standard deviation
VAS - Visual AnalogScale

Tables and figures

Table 1: Sociodemographic and clinical characteristics.

Variable	**N=20**
Age (years), mean (SD)	63.1 (7.76)
Female sex, n (%)	16 (80)
Affected joint, n (%)	
Left	5 (25)
Right	7 (35)
Both	8 (40)
Kellgren-Lawrence grade, n (%)	
II	6 (30)
III	11 (55)
IV	3 (15)
Chronic medical condition, n (%)	13 (65)
Number of prior injections, median (IQR)	2 (2-8)
Injected volumen (ml), median (IQR)	1 (1-2)

Table 2: Chronic medical condition.

Chronic medical condition	N (%)
Hand osteoarthritis*	3 (15)
Osteoporosis*	3 (15)
Diabetes	2 (10)
Chondromalacia*	1 (5)
Gonarthrosis*	1 (5)
Hypercholesterolemia	1 (5)
Hypertension	1 (5)
Palindromicrheumatism*	1 (5)
Rheumatoidarthritis*	1 (5)

** Articular pathology*

Table 3: Concomitant medication.

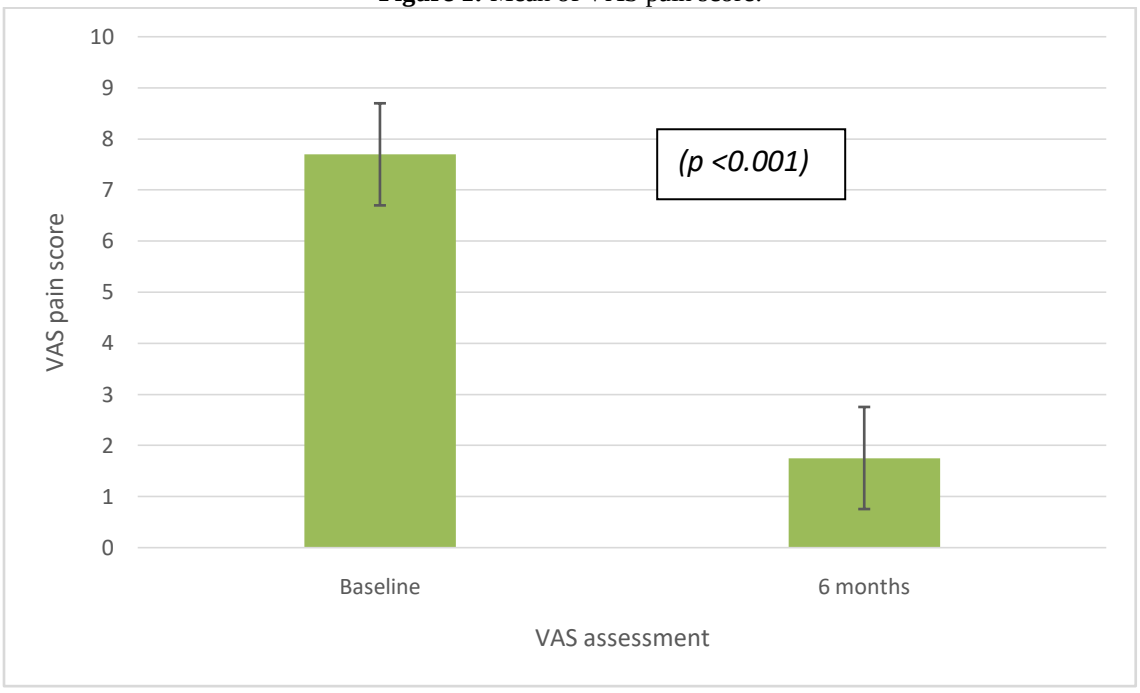
Concomitantmedication	N (%)
NSAIDs	12 (60)
Paracetamol	4 (20)
Nutraceutical	3 (15)
Etanercept	1 (5)

Multiple options possible per patient.

Table 4: Functional assessment.

Adequatefunction	Yes, n (%)	No, n (%)
Key	18 (90)	2 (10)
Grip	19 (95)	1 (5)
Button	17 (85)	3 (15)

Figure 1: Mean of VAS pain score.



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