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Intra-articular hyaluronic acid compared with corticoid injections for the treatment of rhizarthrosis[1]

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Summary

Objective: Prospective assessment of the efficacy and tolerability of intra-articular sodium hyaluronate (SH; Ostenil® *mini*) and triamcinolone acetonide (TA; Volon® A10) for treatment of osteoarthritis (OA) of the carpometacarpal (CMC) joint of the thumb in a 26-week, controlled, randomized, on an intention to treat, masked-observer study.

Methods: Patients were treated with three intra-articular injections of either SH ($n = 28$) or TA ($n = 28$). Primary assessments were pain according to a 100 mm visual analogue scale and extensive clinical and functional parameters such as swelling, grip power and range of motion. The population was analysed using one- and two-sided Mann–Whitney (MW) estimators.

Results: Maximum pain relief occurred at 2–3 weeks for TA and at week 26 for SH after the first intra-articular injection. At weeks 2–3 TA was significantly better than SH (MW: 0.3319 and 0.3063; $P = 0.9827$ and 0.9929). At week 26 a slight superiority of SH could be observed (MW: 0.53; $P = 0.3624$) and non-inferiority could be proven. After 26 weeks lateral pinch power was significantly better in the SH-group (MW: 0.6331; $P = 0.0226$). In all, 88.0% of patients treated with SH and 79.1% of the TA-group described pain improvement after 26 weeks. Both agents were well tolerated. No adverse events with causal connection to the investigational products occurred.

Conclusion: A single course of three SH injections is effective in relieving pain and improving joint function in patients with OA of the CMC joint of the thumb. Although in comparison with triamcinolone its effects are achieved more slowly, the results indicate a superior long-lasting effect of hyaluronan at 6 months after end of treatment period.

Key words: Thumb carpometacarpal osteoarthritis, Rhizarthrosis, Hyaluronic acid, Intra-articular injection, Ostenil Mini, Corticosteroid, Triamcinolone.

Introduction

The age-adjusted prevalence of radiographic osteoarthritis (OA) of the carpometacarpal (CMC) joint of the thumb has been reported to be 7% for men and 15% for women[1]. Among postmenopausal women the radiological prevalence is as high as 33%[2]. Another study showed that in elderly white male individuals 2% of the right and 3% of the left thumbs are affected by symptomatic OA whereas it is found in 5% of both sides among women[3]. By some authors OA of the thumb is considered to be an indicator for a general predisposition towards OA in weight bearing joints[4]. Thumb CMC OA is common but does not necessarily lead to disability[1]. Therefore, it is likely to be underdiagnosed in clinical practice. There is a close association between thumb CMC OA and adipositas, which seems to be due to both the mechanical and systemic metabolic impact of obesity[5].

The symptoms are described to be such as pain, swelling, instability, deformity and loss of motion. Common clinical tests to assess the severity of thumb CMC OA are pulp pinch power and pain as well as lateral pinch power and pain. Thumb CMC OA is classified radiologically after Kellgren 0–4 or Eaton and Glickel I–IV.

Severe disabling forms of thumb metacarpal OA are frequently treated surgically. Among numerous procedures[6] the choice is between trapeziometacarpal arthrodesis and trapezial excision with ligament reconstruction and tendon interposition. Both procedures had similar results with regard to pain, function and satisfaction in a recent study[7], though some authors claim to reserve arthrodesis for posttraumatic arthritis in young patients[8].

Although there exist effective operative techniques, conservative approaches are reported to be of high benefit[9]. Technical accessories, splints, nonsteroidal anti-inflammatory drugs and extensive advice on how to accommodate activities of daily living find their application. One group denied clinical benefit from intra-articular steroid injection

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into the thumb CMC joint[10]. Its treatment with intra-articular injection of hyaluronic acid has not been described, yet.

In synovial fluid hyaluronic acid contributes to the joint homeostasis as one of its primarily critical components[11]. It was shown that in osteoarthritic joints, both the concentration and the molecular weight of intra-articular hyaluronic acid are decreased by depolymerisation. This leads to a reduction of viscoelasticity of the synovial fluid[12]. Several groups started trials on knee joints with the intention to supplement the emptied hyaluronan stores by intra-articular injections[13,14]. It was found that such injections can augment the flow of synovial fluid, normalize the synthesis and inhibit the degradation of endogenous hyaluronic acid, and relieve joint pain[15]. Although some authors showed a lack of efficacy of hyaluronan injection[16], a recent meta-analysis confirms its efficacy and safety for the treatment in OA of the knee[17]. Another meta-analysis ascribes only small effects to intra-articular hyaluronic acid[18]. Preliminary results of joints other than the knee, such as shoulder, hand, hip, temporomandibular joint, spine, foot, and ankle, have been promising and partially confirmed results of treatment of OA of the knee[19]. This study's intention was to determine the effects of intra-articular hyaluronic injections into the osteoarthritic CMC joint of the thumb in comparison with the corticosteroid triamcinolone.

Patients, materials and methods

STUDY SITE AND STUDY'S PERIOD

This randomized, prospective, active-controlled, masked-observer study was based on an intention to treat. The clinical trial was approved by the local ethics committee and follows the Declaration of Helsinki principles. Patients, who had given informed consent, were seen by the main investigators, two orthopaedic surgeons in two centres in the period between August 2001 and December 2003. Patients fulfilling the inclusion criteria and sparing reasons for exclusion were enrolled into the study until the number of 28 patients in each group was achieved. They were treated either with the hyaluronic acid containing compound (Ostenil® *mini*) or the corticosteroid triamcinolone (Volon® A10).

Seven visits were scheduled in total. Patients were seen weekly for the first five appointments, administering the intra-articular injections within meetings 2–4. No anaesthetic was administered prior to injection. During visit 1, patients were checked for exclusion criteria and a wash-out period of analgesics other than paracetamol was initiated. Patients were assessed 3, 14 and 26 weeks after application of the first injection. Assessment was conducted by two masked observers unknowing the outcome of the patients' randomization. The main investigators and observers had received special training in clinical assessment. Baseline assessment was performed before injection. No additional punctures were permitted, when entered the study protocol.

Inclusion criteria

Patients aged between 44 and 80 years showing symptomatic OA of the CMC joint of the thumb associated with radiographic evidence according to the Kellgren Score were included. For the purposes of the study, patients who reported pain (according visual analogue scale (VAS) $\geq$ 40 mm) for at least 6 months, who were in good general condition and good compliance and who had given their written informed consent were included. Many of these patients presented a dissatisfying history of prior treatment attempts, which variably included physical therapy, splints or nutritional supplements and nonsteroidal anti-inflammatory drugs or other oral analgesics, which had to be ceased 1 week before the first injection. All previous treatments and relevant concomitant diseases were recorded and checked for exclusion criteria. Demographic data, such as initials, gender, race, weight, height, age, and nicotine and alcohol uptake were recorded within the baseline visit. Concomitant medications and diseases were updated at each visit. Additional to paracetamol no other oral analgesic was permitted, when entered the study protocol.

Exclusion criteria

The following findings led to exclusion from the study: History or presence of alcohol or drug abuse, psychotic disorders, epilepsy, risk of suicide, subjects unable to understand informed consent or having a high probability of non-compliance, intra-articular treatment of any joint with corticosteroids or glycosaminoglycans within 3 months or with a sodium hyaluronate (SH)-based product within 6 months prior to the first injection. Moreover, patients with known allergy or other contra-indications to administered reagents, critical skin conditions at injection side, hemarthrosis or joint effusion, non-osteoarthritic joint disease (rheumatoid arthritis, inflammatory joint diseases, chondrocalcinosis), immune deficiencies, malignant diseases, uncontrolled diabetes, use of anticoagulants or joint infection were excluded.

Observation time and study's endpoints

Patients were observed for 27 weeks, defining the last visit as the study's endpoint. Study treatment was stopped prematurely if it was the patient's wish to terminate participation or in case of occurrence of adverse effects of intra-articular treatment. As the study was based on an intention to treat, drop outs were not replaced.

SH-group

Ostenil® *mini* (TRB Chemedica AG, Haar; 22.70€ per injection) is a sterile 1 ml pre-filled syringe containing 1% SH destined to be directly injected into the articular cavity. One millilitre isotonic solution contains 10.0 mg SH. Other contents are sodium chloride, sodium monohydrogenphosphate, sodium dihydrogenphosphate and water for injection. The active ingredient, SH, is obtained by fermentation of *Streptococcus zooepidermicus* and is highly purified. No animal proteins are used during fermentation procedure and hence, it has negligible allergenic potential. The average molecular weight of the SH is 1.2 million Dalton. Administration was conducted as recommended by the manufacturer.

Triamcinolone acetonide (TA) group

Commercially available triamcinolone acetonide Volon® A10 (Emra-Med Arzneimittel GmbH, Trittau, Germany; 13.05€ per injection) was used as treatment for the control group. One vial Volon® A10 contains 10 mg triamcinolone acetonide (TA) in 1 ml crystal suspension. They were administered as recommended by the manufacturer.

Intra-articular injections

Injections with the investigational products were only administered by the two main investigators to avoid bias by different treatment techniques. Fluoroscopy or sonography for confirmation of intra-articular injection was not applied.

Effectiveness assessments

Effectiveness assessments were carried out within every visit by one of the two masked observers. Pain was documented using a VAS. Other symptoms recorded were heat, swelling and crepitations under palpation. Function was assessed by lateral (key) pinch grip and pulp pinch grip. Mobility was documented by radial and palmar ab-/adduction and opposition. A screening for local or systemic side effects was conducted at each visit and if necessary recorded.

Statistical methods

This study was based on an intention to treat, which means that all 56 randomized patients who received at least one injection were included into the data set. Homogeneity analysis was performed by calculating the Mann−Whitney (MW) superiority measures, as they are robust (nonparametric) and standardised measures of difference. In addition, their two-sided 90% confidence intervals (CI) were regarded as a tool for testing equivalence (two-sided, unidirectional) on the two-sided level $\alpha = 0.05$ (Fig. 1).

The MW estimator for the demographic−anamnestic criteria (interpretation according to Cohen) is expressed in values between 0 and 1. Relevant benchmarks of the effect sizes (MW) for demographic and anamnestic criteria are the following: 0.5: equality; 0.44 and 0.56: small differences; 0.36 and 0.64: medium-sized differences; 0.29 and 0.71: large differences. As benchmark for statistically significant group differences an MW estimator of 0.36 and 0.64 will be applied in this study. Moreover, differences were considered as statistically significant when $P < 0.05$. The influence of such baseline inhomogeneities upon effectiveness results was analysed by means of supportive stratified analyses in the sense of a sensitivity analysis.

For better interpretation of homogeneity, relevant baseline criteria were grouped as demographic criteria (gender and age), anamnestic criteria (morning stiffness, crunch, pain at rest, pain on motion, pain in other joints, impairment of function, previous therapies, Kellgren Score) and effectiveness criteria (VAS pain, radial and palmar abduction, opposition, swelling, heat, pain on pressure, crepitation, pulp pinch and lateral pinch strength (impairment), pulp pinch and lateral pinch pain, paracetamol consumption/week, and the global clinical impression due to investigator's and patient's rating).

For the confirmatory analysis the one-sided Wilcoxon−Mann−Whitney-test was used as a test for non-inferiority and superiority. The medical relevance of differences between groups was quantified using as corresponding effect size the MW superiority measure and its one-sided 97.5% CI. The MW-measure (0.0−1.0) gives the probability that a randomly selected patient of the test group is better off than a randomly selected patient of the comparator group. Benchmark values were defined and applied as mentioned above.

For the comparison purposes the MW superiority measures were calculated as robust (nonparametric) and standardised measures of difference, which can be applied on all types of data, all distributions and all types of relevant differences.

Quantitative absolute variables were described in terms of the average and the standard deviation, percent changes and in median values being the more robust statistic in case a distribution is skewed. The database was not large enough to assess whether there were differences in effects with respect to age, gender or other subgroups.

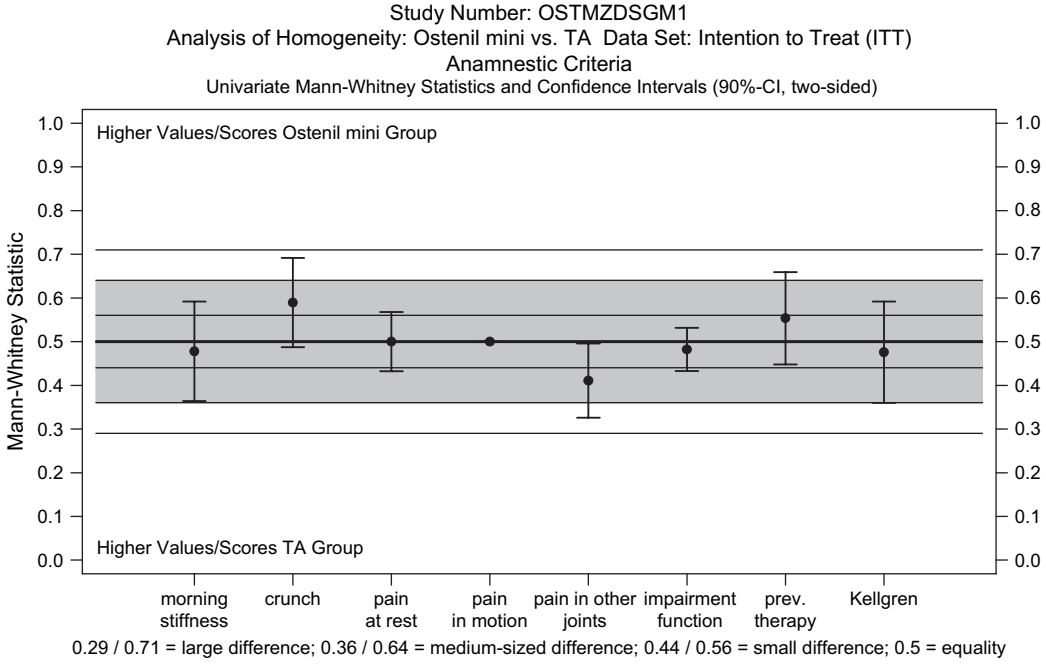

Fig. 1. Results of analysis of homogeneity for the anamnestic criteria with univariate MW estimators and their two-sided 90% CI. The shaded area indicates the range of equivalence (non-relevant group differences).

Results

ANALYSIS OF HOMOGENEITY

Only small or medium-sized differences (MW test) between the SH-group and the triamcinolone-group (TA) were found with respect to gender (MW: 0.4107, lower bound CI: 0.3137, upper bound CI: 0.5639, *P*-value: 0.4362) and age (MW: 0.4388, lower bound CI: 0.3256, upper bound CI: 0.4958, *P*-value: 0.1771). All in all 11 male and 45 female subjects were analysed. The median age was 59.5 in the SH-group and 61.0 in the TA-group (Table I). The SH-group comprised 14 cases on each side. Fifteen left and 13 right CMC joints were treated in the TA-group.

No relevant differences were found among the anamnestic criteria, such as morning stiffness, crunch, pain at rest and in motion, pain in other joints, impairment of function, previous therapy and the radiographic severity following the Kellgren scale (Table I). Moreover, there were no substantial differences concerning functional effectiveness criteria such as range of motion (radial and palmar abduction and opposition), and arthritic symptoms such as swelling, local hyperthermia, pain on pressure crepitations and others (Table II). Among the functional analysis the biggest difference was found with respect to lateral pinch pain, with more patients in the TA-group. Nevertheless, all functional tests showed an equal distribution between both groups as well as parameters as paracetamol demand and the pain intensity reported by the patient and estimated by the physician. All in all, the two groups correspond in largest extent.

Among the patients 11 male and 45 female subjects were analysed. With a mean of 2.1 and a median of 2.0 the Kellgren Score was equally distributed in both groups. The highest number of patients was found in stadium 2 (50% of the patients). Within the SH-group OA affected equally 14 left and right CMC joints whereas in the TA-group 15 left and 13 right were observed.

The primary criterion of effectiveness was pain, assessed by using the visual analogue pain grading scale according to Huskisson (VAS: 0 = no pain, 100 = worst imaginable pain). Analysis of VAS according to MW statistics and appropriate CI demonstrate inferiority of SH-group (superiority of TA-group) up to week 14. In week 26 a slight superiority of SH-group could be observed and non-inferiority could be proven statistically significant (Fig. 2). The development of pain scores is expressed in Table III. For reduction of outlier's impact, pain scores are expressed as median rather than mean values. Expressed in percent the long-term pain relief according to the VAS scale after 26 weeks was 56% within the SH-group and 22.6% in the TA-group. Triamcinolone showed a faster onset of pain relief with a maximum at 2 and 3 weeks after the first injection, which was significantly better than SH (MW: 0.3319 and 0.3063; $P = 0.9827$ and 0.9929). Among patients of the SH-group inset of pain relief was more moderate and reached its maximum after 26 weeks. Every reduction/increasing (regardless to what extent) of VAS was rated as improvement/worsening. It could be observed that the number of patients with improvement was steadily increasing in the SH-group until the long-term observation after 6 months. In the TA-group the number of patients with improvement was increasing until week 3 but decreasing in the visits after 14 and 26 weeks. An alternative pain evaluation using an ordinal pain rating scale from 0 to 4 documented comparable results with respect to the time-dependent effect of pain relief.

Table I
Homogeneity of demographic and anamnestic criteria, MW variables

Criterion	MW	Lower bound CI	Upper bound CI	*P*-value
Gender	0.4107	0.3137	0.5639	0.4362
Age	0.4388	0.3256	0.4958	0.1771
Morning stiffness	0.4777	0.3638	0.5916	0.8077
Crunch	0.5893	0.4871	0.6915	0.2588
Pain at rest	0.5	0.432	0.568	1
Pain in motion	0.5	0.5	0.5	1
Pain in other joints	0.4107	0.3256	0.4958	0.1771
Impairment of function	0.4821	0.4328	0.5315	1
Previous therapy	0.5536	0.4478	0.6593	0.5815
Kellgren score	0.4758	0.3597	0.5918	0.7539

Table II
Homogeneity of baseline effectiveness criteria, MW variables

Criterion	MW	Lower bound CI	Upper bound CI	*P*-value
VAS pain (mm)	0.4751	0.3509	0.5993	0.7541
Radial abduction	0.4866	0.3622	0.611	0.8674
Palmar abduction	0.4082	0.2848	0.5315	0.2399
Opposition	0.4662	0.3441	0.5883	0.6689
Swelling	0.4107	0.3154	0.5061	0.227
Heat	0.4821	0.3741	0.5902	1
Pain on pressure	0.5179	0.489	0.5467	1
Crepitation	0.5179	0.4306	0.6051	1
Pulp pinch power	0.5165	0.4531	0.58	1
Lateral pinch power	0.4107	0.3154	0.5061	0.227
Pulp pinch pain	0.4821	0.4328	0.5315	1
Lateral pinch pain	0.375	0.2864	0.4636	0.055
Paracetamol consumption (per week)	0.4821	0.4196	0.5447	1
Pain intensity (investigator)	0.4751	0.3631	0.5871	0.8043
Pain intensity (patient)	0.4758	0.3624	0.5891	0.7792

The joint function was assessed within every visit. The focus of this study lies on the final examination after 26 weeks (Table IV). Using the univariate MW estimators and their one-sided 97.5% CI (α was adjusted to 0.025) the lateral pinch (key grip) strength showed equality between treatment groups. After 6 months of treatment moderate superiority of the SH-group was found (MW: 0.6331, lower bound CI: 0.5273, *P*-value: 0.0226). After 6 months 52.0% of the SH-group and 42.3% of the TA-group patients reported improvement. Lateral pinch pain showed equality of treatment groups from weeks 1 to 14 and a slight superiority of SH-group after 6 months (MW: 0.5731, lower bound CI: 0.4526, *P*-value: 0.1966).

Assessment of the pulp pinch power showed equality of treatment groups at week 2. For all other visits small to medium superiority of SH-group could be observed (week 26: MW: 0.6062, lower bound CI: 0.474, *P*-value: 0.1045). For pulp pinch pain equality could be observed in weeks 2, 3 and 26. In weeks 4 and 14 superiority of TA-group could be observed (week 3: MW: 0.3618, lower bound CI: 0.2412, *P*-value: 0.9934). At the end of the study improvement of pulp pinch pain could be obtained for 72% of the patients in the SH-group and 34.6% of the TA-group.

For radial abduction from week 1 to week 14 equality or rather small superiority of TA-group could be observed. At week 26 a small superiority for the SH-group could be found (Table IV). With respect to palmar abduction for weeks 1–3 small and for weeks 14–26 medium relevant superiority of the SH-group could be observed. For opposition small

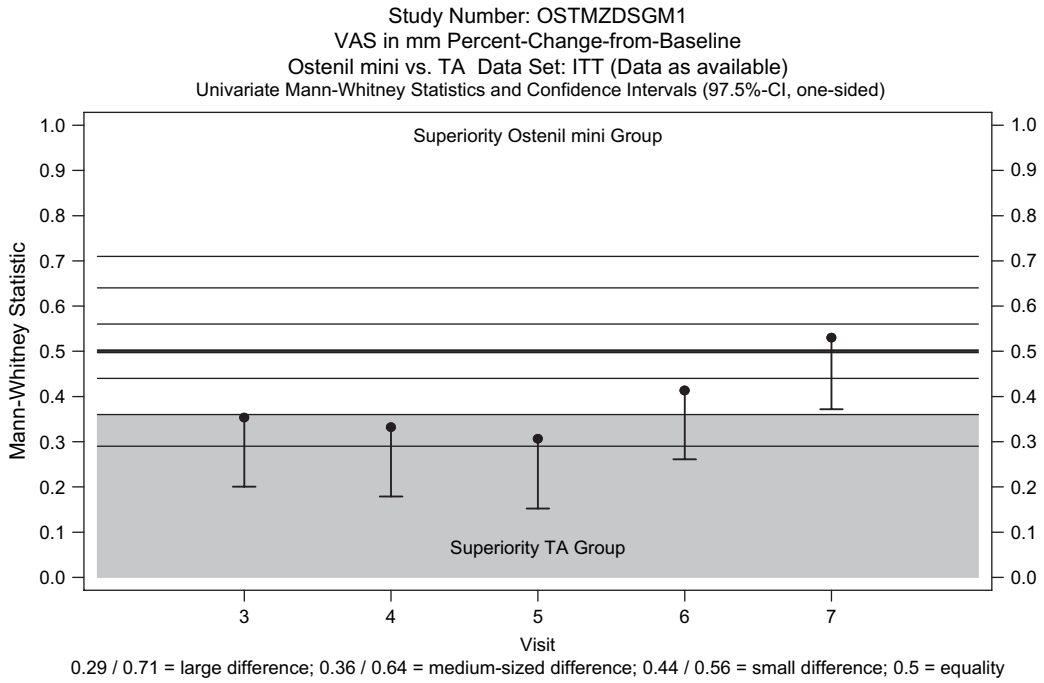

Fig. 2. The results of the analyses of non-inferiority for the primary effectiveness criterion VAS pain with univariate MW estimators and their one-sided 97.5% CI (α was adjusted to 0.025).

superiority of the SH-group was found throughout the study except week 2. This superiority was relevant in weeks 14 and 26.

For swelling from weeks 1 to 14 superiority of TA-group could be observed. After 6 months superiority of SH-group could be observed and non-inferiority could be proven. Heat was observed to be slightly superior in the SH-group from week 3. For pain on pressure starting from observed equality in week 1, superiority of TA-group was steadily increasing till week 14. After half a year both treatment groups ended in equality. For crepitation in all visits equality up to small superiority for the SH-group could be observed.

Effectiveness was assessed based on a Clinical Global Impression (CGI) rating scale completed by investigator and patients in the last follow-up visit. Evaluation was encoded from 1 to 5 (very good/without complaints−worsening). Medium/relevant superiority of SH-group could be observed for the investigator's judgement of CGI and small superiority for patient's judgement. In both cases non-inferiority of the SH-group could be proven.

Concerning the paracetamol consumption, equality for both treatment groups was found from weeks 1 to 3 and after 6 months. In week 14 a slight superiority of triamcinolone was observed.

Adverse events occurred in four (14.3%) subjects within each treatment group. Causal connection to the investigational products was negated by the investigators in all cases. Five adverse events (three in SH-group and two in TA-group: e.g., collapse, pain in index; lumbal ischialgia and lung carcinoma) caused the early withdrawal of subjects from study. Incidents and near incidents which led to death or led to a serious deterioration (life-threatening illness or injury; permanent impairment of a body function or permanent damage to a body structure; a condition necessitating medical or surgical intervention to prevent permanent impairment of a body function or permanent damage to a body structure) in the state of health of a patient, user or other person did not occur.

Table III
Total values of VAS pain assessment (in mm from the left of a horizontal line with a range 0−100 mm)

	SH-group (median and number)	TA-group (median and number)
Visit 1	65.5, $n = 28$	63.5, $n = 28$
Visit 2	64.5, $n = 28$	61.5, $n = 28$
Visit 3	54.0, $n = 26$	46.0, $n = 27$
Visit 4	41.0, $n = 26$	33.0, $n = 27$
Visit 5	34.0, $n = 26$	20.0, $n = 27$
Visit 6	35.0, $n = 26$	22.0, $n = 27$
Visit 7	30.0, $n = 25$	45.5, $n = 26$

Discussion

The data illustrate the effectiveness of both hyaluronic acid and triamcinolone in the treatment of OA of the CMC joint of the thumb. In all, 88.0% of the patients treated with SH and 79.1% of those treated with triamcinolone described improvement of pain, 26 weeks after first treatment. Both drugs relieved clinical symptoms such as pain, lack of function and loss of motion range. Triamcinolone showed a faster onset of pain relief with a maximum at 2 and 3 weeks after initiation of treatment. Towards the end of the study its positive effects were decreasing. Similar findings were made by Caborn *et al.*[20] in the treatment of OA of the knee joint. Among patients of the SH-group inset of pain relief was more moderate and reached its maximum after 26 weeks. Similar observations could be made for other parameters such as swelling of the joint. For the lateral pinch (key grip) strength and lateral pinch pain after 6 months of treatment moderate superiority of the SH-group

Table IV
Effectiveness criteria 26 weeks after first application (visit 7) (SH-group: n = 25; TA-group: n = 26)

Criterion	MW	Lower bound CI	*P*-value	Improvement SH (%)	Improvement TA (%)
VAS pain (mm)	0.53	0.3719	0.3624	88.0	79.2
Lateral pinch power	0.6331	0.5273	0.0226	52.0	42.3
Lateral pinch pain	0.5731	0.4526	0.1966	68.0	30.8
Pulp pinch power	0.6062	0.474	0.1045	40.0	28.0
Pulp pinch pain	0.53	0.3933	0.4411	72.0	34.6
Radial abduction	0.5354	0.3807	0.3354	92.0	88.5
Palmar abduction	0.6323	0.4757	0.0532	88.0	76.9
Opposition	0.6125	0.4521	0.0896	92.0	73.1
Swelling	0.5908	0.4607	0.1467	60.0	34.6
Heat	0.5385	0.4872	0.2549	44.0	34.6
Pain on pressure	0.5054	0.3829	0.5894	28.0	26.9
Crepitation	0.4977	0.4092	0.6852	72.0	73.1
Paracetamol consumption (per week)	0.4992	0.4459	0.7647		
CGI investigator	0.6246	0.4811	0.0545	88.5	80.8
CGI (patient)	0.5608	0.4131	0.2346	65.4	57.7

was found. For palmar abduction, opposition and pulp pinch power moderate superiority of SH was observed throughout the study. The theoretical background of SH implicates that its therapeutic success is not due to symptomatic pain relief, but due to regeneration of viscoelasticity of the synovial fluid by refilling the emptied hyaluronan stores.

Corticoid phobia by both patients and doctors should not be underestimated. Therefore, SH offers an effective alternative. Meenagh *et al.*[10] stated that in their study triamcinolone could not be proven to be beneficial in rhizarthrosis compared with placebo injection. They report statistically significant improvements in patient and physician global assessments at weeks 4, 12, and 24 in the placebo group and at weeks 4 and 12 in the steroid group indicating a strong placebo or self-limiting effect. Moreover, none of the groups showed improvement in the VAS of pain at 24 weeks. Contrarily our data clearly illustrate strong positive short- and moderate long-term effects of triamcinolone. Expressed in percent the long-term pain relief according to the VAS scale after 26 weeks was 22.6% in the TA-group compared with 56% within the SH-group.

Unfortunately, it was not possible to assess patients for longer than 6 months. A further long-term follow-up would be of great interest. It must be admitted that the study lacks a placebo group. Data collection was done by orthopaedists who delivered therapy. This could be regarded as a possible source of bias. This data cannot be compared with that of others studies easily because of the lack of an international assessment score for the thumb CMC joint. No confirmative diagnostics were made to assure that intra-articular injections were appropriately placed, e.g., with ultrasound or fluoroscopy. It is likely that para-articular injection finally affects both, TA- and SH-group equally. A risk of statistical bias is carried by the fact that para-articular TA might ameliorate symptoms of rhizarthrosis. In contrast SH should be injected strictly intra-articularly to be beneficial. Although an obvious tendency towards superiority of SH in comparison with triamcinolone was observed, in the majority of the assessed parameters differences lack statistical significance.

A disadvantage of SH treatment is the necessity of three intra-articular injections carrying the risk of iatrogenic infection. Moreover, its effect latency can cause dissatisfaction among patients. Treatment with three injections of SH (68€) is pricier than triamcinolone (39€).

Until today, there are no data suggesting what the exact dosing regimen of SH injections should be. It is believed that better results could be achieved by administering an optimal regimen.

With respect to the long-term results, SH seems to be the better alternative in treatment of the OA of the thumb CMC joint. In comparison with triamcinolone it shows slide to moderate superiority in almost all the assessed clinical parameters after 6 months with significant superiority in lateral pinch pain.

References

1. Haara MM, Heliovaara M, Kroger H, Arokoski JP, Manninen P, Karkkainen A, *et al*. Osteoarthritis in the carpometacarpal joint of the thumb. Prevalence and associations with disability and mortality. J Bone Joint Surg Am 2004;86-A(7):1452–7.
2. Armstrong AL, Hunter JB, Davis TR. The prevalence of degenerative arthritis of the base of the thumb in postmenopausal women. J Hand Surg [Br] 1994;19(3): 340–1.
3. Zhang Y, Niu J, Kelly-Hayes M, Chaisson CE, Aliabadi P, Felson DT. Prevalence of symptomatic hand osteoarthritis and its impact on functional status among the elderly: The Framingham Study. Am J Epidemiol 2002; 156(11):1021–7.
4. Hochberg MC, Lane NE, Pressman AR, Genant HK, Scott JC, Nevitt MC. The association of radiographic changes of osteoarthritis of the hand and hip in elderly women. J Rheumatol 1995;22(12):2291–4.
5. Cicuttini FM, Baker JR, Spector TD. The association of obesity with osteoarthritis of the hand and knee in women: a twin study. J Rheumatol 1996;23(7): 1221–6.
6. Martou G, Veltri K, Thoma A. Surgical treatment of osteoarthritis of the carpometacarpal joint of the thumb: a systematic review. Plast Reconstr Surg 2004;114(2):421–32.
7. Hartigan BJ, Stern PJ, Kiefhaber TR. Thumb carpometacarpal osteoarthritis: arthrodesis compared with ligament reconstruction and tendon interposition. J Bone Joint Surg Am 2001;83-A(10):1470–8.
8. Carroll RE. Arthrodesis of the carpometacarpal joint of the thumb. A review of patients with a long postoperative period. Clin Orthop 1987;220:106–10.

9. Berggren M, Joost-Davidsson A, Lindstrand J, Nylander G, Povlsen B. Reduction in the need for operation after conservative treatment of osteoarthritis of the first carpometacarpal joint: a seven year prospective study. Scand J Plast Reconstr Surg Hand Surg 2001;35(4): 415–7.
10. Meenagh GK, Patton J, Kynes C, Wright GD. A randomised controlled trial of intra-articular corticosteroid injection of the carpometacarpal joint of the thumb in osteoarthritis. Ann Rheum Dis 2004;63(10):1260–3.
11. Laurent TC, Fraser JR. Hyaluronan. FASEB J 1992; 6(7):2397–404.
12. Balazs EA, Watson D, Duff IF, Roseman S. Hyaluronic acid in synovial fluid. I. Molecular parameters of hyaluronic acid in normal and arthritis human fluids. Arthritis Rheum 1967;10(4):357–76.
13. Peyron JG. Intra-articular hyaluronan injections in the treatment of osteoarthritis: state-of-the-art review. J Rheumatol Suppl 1993;39:10–5.
14. Peyron JG. A new approach to the treatment of osteoarthritis: viscosupplementation. Osteoarthritis Cartilage 1993;1(2):85–7.
15. Rydell N, Balazs EA. Effect of intra-articular injection of hyaluronic acid on the clinical symptoms of osteoarthritis and on granulation tissue formation. Clin Orthop 1971;80:25–32.
16. Henderson EB, Smith EC, Pegley F, Blake DR. Intra-articular injections of 750 kD hyaluronan in the treatment of osteoarthritis: a randomised single centre double-blind placebo-controlled trial of 91 patients demonstrating lack of efficacy. Ann Rheum Dis 1994; 53(8):529–34.
17. Wang CT, Lin J, Chang CJ, Lin YT, Hou SM. Therapeutic effects of hyaluronic acid on osteoarthritis of the knee. A meta-analysis of randomized controlled trials. J Bone Joint Surg Am 2004;86-A(3):538–45.
18. Lo GH, LaValley M, McAlindon T, Felson DT. Intra-articular hyaluronic acid in treatment of knee osteoarthritis: a meta-analysis. JAMA 2003;290(23): 3115–21.
19. Kelly MA, Moskowitz RW, Lieberman JR. Hyaluronan therapy: looking toward the future. Am J Orthop 2004; 33(2 Suppl):23–8.
20. Caborn D, Rush J, Lanzer W, Parenti D, Murray C. A randomized, single-blind comparison of the efficacy and tolerability of hylan G-F 20 and triamcinolone hexacetonide in patients with osteoarthritis of the knee. J Rheumatol 2004;31(2):333–43.