12th Annual Meeting
European Orthopaedic Research Society (EORS)
Lausanne, October 10-13, 2002

Intra-articular hyaluronic acid for nonradicular low back pain

A randomised, controlled, blind-observer clinical study

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Aim

To investigate the efficacy and safety of intra-articular sodium hyaluronate (SH) compared with an intra-articular glucocorticoid (triamcinolone acetonide, TA) in the treatment of chronic lumbar pain of nonradicular origin

Rationale

Facet joints are synovial joints in a capsule, like the knee joint. Chronic „low back pain“ mainly results from osteoarthritis of those joints. Standard treatment includes administration of plain analgesics or NSAIDs. Nerve blockade with local anaesthetics, and peri-/intra-articular treatment of facet joints with local anaesthetics and/or corticoids are also commonly used. Regarding the contraindications, possible side-effects and interactions of glucocorticoids and analgesics, it would be desirable to establish a more “natural” long acting therapy with a better benefit/risk ratio.

The biopolymer hyaluronic acid (SH) is an essential component of the synovial fluid and plays an important role in protection and metabolism of the joint cartilage. Viscosupplementation with SH has been shown to have a favourable effect on pain and restricted joint mobility in patients with knee osteoarthritis by several investigators. Therefore, we decided to investigate the efficacy of SH in comparison with a standard corticoid (TA) in the treatment of osteoarthritis of facet joints.

Patients

60 patients with chronic, nonradicular low back pain randomly assigned into 2 groups

Table 1: Demographic Data

	Age (years)	Height (cm)	Weight (kg)	Sex
SH group	64.97 ± 8.31	168.97 ± 7.90	74.31 ± 12.40	18 f, 12 m
TA group	65.87 ± 9.79	166.68 ± 7.76	72.89 ± 12.57	24 f, 6 m

Methods and Material

Test products:
- 10 mg sodium hyaluronate (Ostenil® mini pre-filled syringes) / facet joint
- 10 mg triamcinolone acetonide / facet joint

Treatment protocol:
- injection of investigational products in facet joints under CT control
- treatment of three subsequent „levels“ (S1 to L3)
- injection in weekly intervals (table 2)

Assessment of pain severity:
- Huskisson 100 mm visual analogue scale for pain (VAS)

Assessment of improvement in function and quality of life:
- Roland Morris Questionnaire (RMQ)
- Oswestry Disability Questionnaire (ODQ)
- Low Back Outcome score (LBOS)
- SF-36

Statistical analysis:
- Standardised differences (=Diff/s) for VAS scale
- Mann-Whitney Statistic and Confidence-Interval (97,5%-CI, one-sided) for RMQ, ODQ and LBOS

Table 2: Examinations / Treatment over Time

	Timepoint	Treatment, Examinations, Patient questionnaires
Visit 1 (V1)	Baseline	Clinical and radiological findings before treatment, inclusion and exclusion criteria, randomisation to treatment group VAS, RMQ, ODQ, LBOS, SF-36
Visit 2 (V2)	7 ± 1 Days after Visit 1	1st injection (S1-L5) Efficacy and tolerability VAS, RMQ, ODQ, LBOS, SF-36
Visit 3 (V3)	7 ± 1 Days after Visit 2	2nd injection (L5-L4) Efficacy and tolerability VAS, RMQ, ODQ, LBOS, SF-36
Visit 4 (V4)	7 ± 1 Days after Visit 3	3rd injection (L4-L3) Efficacy and tolerability VAS, RMQ, ODQ, LBOS, SF-36
Visit 5 (V5)	7 ± 1 Days after Visit 4	Efficacy and tolerability VAS, RMQ, ODQ, LBOS, SF-36
Visit 6 (V6)	90 ± 3 Days after Visit 4	Efficacy and tolerability VAS, RMQ, ODQ, LBOS, SF-36
Visit 7 (V7)	180 ± 3 Days after Visit 4	Efficacy and tolerability VAS, RMQ, ODQ, LBOS, SF-36

Results (1)

In both treatment groups joints at level 5 had higher mean Kellgren scores compared to the L3 joints, suggesting that in general lower joints may present more severe degeneration

Table 3: Severity of osteoarthritis (Kellgren)

	L3 right	L3 left	L4 right	L4 left	L5 right	L5 left	
SH group	2.41± 0.82	2.28± 0.75	2.90± 0.90	2.90± 0.82	3.21± 0.69	3.21± 0.79	Mean score
TA group	2.57± 0.74	2.57± 0.74	2.96± 0.75	3.04± 0.85	3.36± 0.76	3.29± 0.79	

Results (2)

1) No unexpected or adverse events were reported in both treatment groups

2) The efficacy of hyaluronic acid was comparable to that of the standard treatment with TA:

a) SH and TA caused a marked decrease in severity of pain (VAS, 40.1% vs. 56.2%) (figure 1). Statistical analysis did not show non-inferiority of SH to TA

b) Both treatments show ed a similar improvement in function. Onset of activity was a bit faster for TA, but SH performed consistently better in the carry-over effect
- Improvement at the end of the study was 43.2% vs. 33.4% in the RMQ for the SH group compared to TA (figure 2)
- Improvement illustrated by the ODQ was 39.1% for SH vs. 29.5% for TA at the end of the study (figure 3)
- LBOS values showed an improvement in quality of life at the end of the study of 43.9% for SH and 34.8% for TA (figure 4)
- Exploratory statistical analysis of physical function and quality of life proved non-inferiority of the SH group in comparison to the TA group (figure 5)

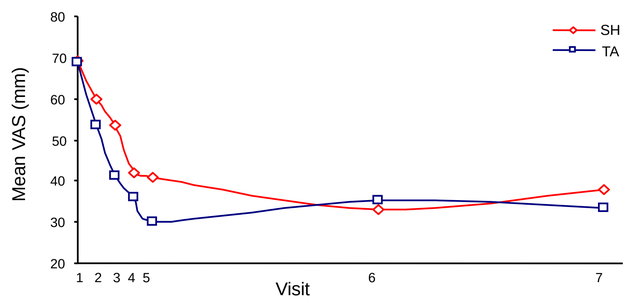


Figure 1: Decrease in pain over time (VAS pain)

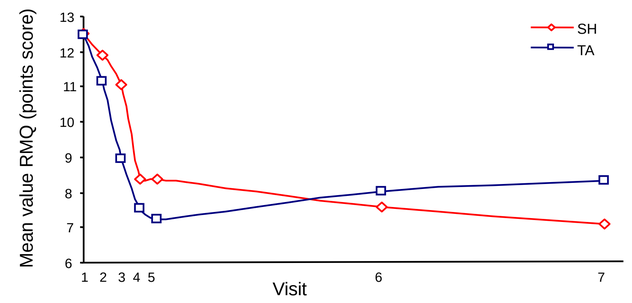


Figure 2: Increase in physical function using the Roland Morris Questionnaire

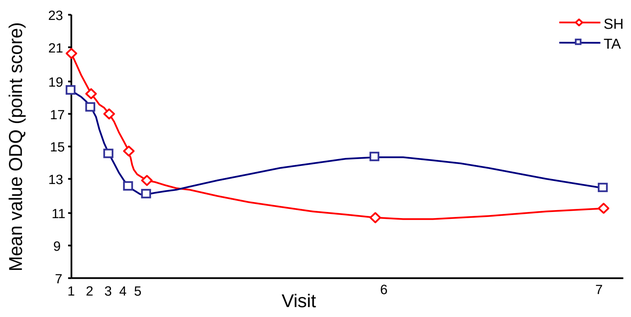


Figure 3: Decrease in pain-induced functional impairment using the Oswestry Disability Questionnaire

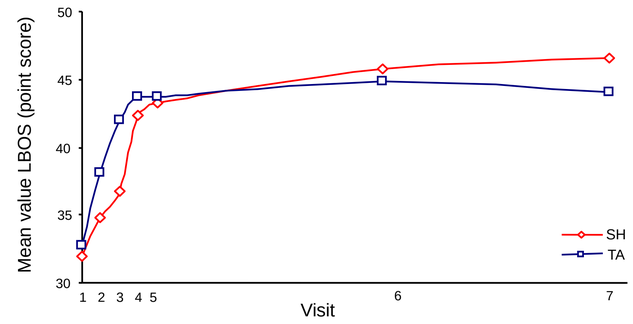
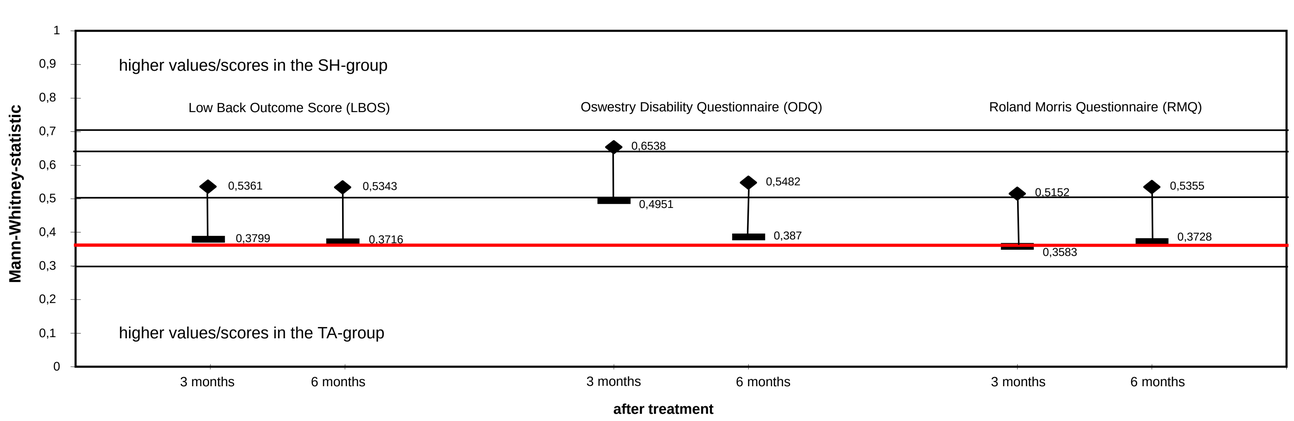


Figure 4: Increased physical function using the Low Back Outcome Score

Figure 5: Exploratory statistical analysis for Low Back Outcome score, Oswestry Disability and Roland Morris Questionnaires



0,29 pronounced inferiority, 0,36 mean inferiority = benchmark of non-inferiority, 0,44 small inferiority, 0,50 equality = bench-mark for superiority, 0,56 small superiority, 0,64 mean superiority, 0,71 pronounced superiority, acc. to Cohen (effect-size d).

Conclusion

The intra-articular treatment of facet joints (levels S1-L5, L5-L4, L4-L3) with SH (Ostenil® mini) in patients with chronic nonradicular pain in the lumbar spine, resulted in a marked reduction in pain with improved function and a better quality of life which was at least equal to the effect of a course of TA injections. SH-treated patients showed greater benefits in the long-term from this treatment. The benefit-risk analysis is definitely in favour of the SH treatment, not least due to the restrictions on the use of TA. Thus intra-articular SH is a very promising new option for the treatment of patients with chronic lumbar symptoms of nonradicular origin.